The New England
Journal of Medicine

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VOLUME 228 JUNE 3, 1943 NUMBER 22

THE UNIVERSALITY OF A SPECIALTY*

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BOSTON

IT HAS been said that a specialist is one who knows more and more about less and less. It has not but might have been said as well that a general surgeon, medical man or practitioner is one who knows less and less about more and more. Although neither of these definitions is to be taken literally, there is enough truth in them to warrant an attempt to estimate just how special a specialty is and how general a practitioner or surgeon should be. I can speak only about one specialty, — neurosurgery, — but I believe that any conclusions concerning the universality of that one will be found to apply with only minor modifications to all others.

Neurological surgery at its birth was the surgery of tumors of the central nervous system. Its father was unquestionably Harvey Cushing, and among its ancestors are found such men as Abernethy, Von Bergmann, Kocher, Kroenlein, Koenig, Mueller, Doyen, Horsley and others too numerous to mention and doubtless of equal importance. Other near relatives — uncles, perhaps — were Elsberg, de Martel and Frazier. The latter with Spiller took the first step toward broadening the scope of this specialty by demonstrating a practical method of dealing with pain in certain regions. The added breadth was not great, however, and neurosurgery remained for years, and indeed is still thought by many to be, pre-eminently the surgery of tumors of the nervous system.

Because they were engaged in pioneering, and because of lack of faith in the explorers as well as lack of intelligent interest on the part of other specialists, the first neurosurgeons had to practice a great deal more than surgery. First of all, they had to be neurologists. The differential diagnosis of an intracranial tumor was not then the relatively simple procedure it is today, complicated though this may be. Nor was the existence of many of the strictly neurologic entities as possible causes of tumorlike symptoms known or suspected by the general practitioners and surgeons who first saw such patients at the start of the twentieth century. Ophthalmoscopy was handicapped by the crude method of obtaining light for the examination. It was practiced only by "eye men," to many of whom a choked disk meant optic neuritis and nothing else. The study of the pathology of the central nervous system, except for the grossest kind, was in its infancy, and a knowledge of the histology of cerebral neoplasms did not exist. Finally, along with any therapy of these tumors went the need for continual revision of what was then known about the physiology of the central nervous system. The burden of all this lay directly on the shoulders of the neurosurgeon. If he failed or refused to carry it, his diagnosis went wrong and his operations were performed too late or in the wrong place, or for conditions that only simulated tumors. Lack of adequate post-mortem studies of the brain led him astray in as yet unoperated living patients, and the apparently contradictory data thus obtained had to be rationalized in the physiologic laboratory. The early neurosurgeons, then, in addition to being highly skilled technicians and competent general surgeons, had also to be their own medical man, ophthalmologist, neurologist, pathologist and physiologist. This made a tremendous demand on their time and energy and constrained them to limit their interest to those patients whose study along such broad lines would most repay them. Obviously these conditions were best met by relatively circumscribed lesions such as tumors, and by the physiologically experimental kind of surgery that had to be practiced for the relief of pain in isolated areas of the body. For all these various reasons, therefore, neurosurgery at its start and until the beginning of World War I was practically limited to the treatment of tu-

*Read before the annual meeting of the Tufts College Medical School Chapter of Alpha Omega Alpha, Boston, December 4, 1942.

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mors of the central nervous system and to the relief of pain.

What of the general men at this time? By general men I mean the general surgeons, the general medical men and the general practitioners. This was the "golden age of surgery." Asepsis had replaced antisepsis, and a knowledge of physiology was supplementing the astounding anatomical proficiency that was then the pride of the profession. The abdominal cavity could now be freely opened and the bowel dealt with without contamination of the peritoneum. Surgery of the prostate and bladder, the thyroid gland and malignant disease was making rapid strides. Patients were finally learning that going to the hospital was not a method of committing suicide and that surgical procedures when carried out in the home, although more convenient for visiting friends and relatives, were disrupting to members of the immediate family and dangerous to themselves. In medicine, the shotgun prescription was coming to be discarded, and not long afterward a period of therapeutic nihilism developed. Such radical departures as the writing of prescriptions in legible English instead of in Latin was another symptom of medical realism. Medicine, too, began to be less anatomic and more physiologic. The value of the hospital also became apparent in nonoperative patients, and the physician came to rely more and more on the consultative opinions of his surgical colleagues, and vice versa. The general practitioner, being almost always without hospital facilities, had to be both surgeon and medical man. He learned about the progress being made in his profession secondhand and developed a tremendous initiative, inventiveness and physical stamina, as well as a sense of his own enforced intellectual inadequacy. With the change of the public's point of view toward hospitals, he was in the forefront of the move to build more of them and to make more use of those that were already available. In this way his work was lightened and done better. Furthermore, he soon found that the local hospital was a magnet that drew surgeons and medical men from the large centers so that he could "tap their brains," profit by their demonstrations, and bring himself more nearly up to date, while giving better care to as many patients as he had always had, or even more.

All these general men, as the numbers and efficiency of hospitals grew, found that because of their availability in emergencies they must be prepared to deal more and more with trauma. In its very nature this meant diagnosing and caring for injuries to the bony skeleton and its contained organs, the brain and spinal cord, the body cavities and their contents, and the coverings of the extremities, such as the muscles, blood vessels and peripheral nerves. Thus a part of what should have been neurosurgery was kept separate from that specialty, partly because of the preoccupation of the neurosurgeon with tumors and pain, and partly because the public by its use of the hospitals forced the general man to assume responsibility for the diagnosis and care of the results of injuries to the central and peripheral nervous system.

These and other forces gradually made general specialists of the surgeon and the general practitioner, and forced them to learn how to deal with any surgical problem that arose. My father, John C. Munro, for example, was most interested in the stomach and duodenum and did most of his significant work with them. His experience was sufficiently great, however, so that in 1902 he wrote a paper on subdural hematomas, in which he advocated what is now recognized as the best modern therapy of these clots, and in 1899 and 1904 others on the efficacy of laminectomy in spinal injuries. He also held and published strong views on the therapy of malignant disease, surgical infections of the kidneys and portal infections associated with appendectomy. In addition, he worked out and first published the principles underlying the modern method of ligating the ductus arteriosus and in 1907 reported a case of attempted ligation of the abdominal aorta for aneurysm. A. J. Ochsner did a hysterectomy, amputated a lobe of the liver, removed a toxic goiter, dissected a neck, and avulsed the sensory root of a gasserian ganglion with equal nonchalance and, except for the latter, with a skill and dexterity that can scarcely be matched today. Samuel J. Mixter, father of one of the distinguished neurosurgeons of today, and Dr. Fred B. Lund, the present senior surgeon of Boston, had the same versatility; the ability of Maurice Richardson and the Mayo brothers in every surgical field is well known.

Such, then, was the approximate situation when World War I broke out in 1914. Surgeons were general surgical specialists, and were expected to do, and did do, any kind of surgery in any part of the body. Such specialists as the neurosurgeons with their tumors, the orthopedists with their tuberculous spines and flat feet, the nose-and-throat men with their mastoids and the dentists with their tooth extractions were regarded for the most part as necessary evils who must be countenanced because of their occasional invaluable aid in a problem that the general surgeons or practitioners were not able to solve alone. As was pointed out at the start, the specialist of that era was

indeed a man who knew more and more about less and less.

After the war it soon became generally apparent that the accumulation of knowledge about the effect of trauma on the body was far exceeding the ability of the general surgeon to absorb it all. Both he and the specialist had to revise their ideas. In neurosurgery intimate knowledge of how to deal with tumors of the central nervous system had been of little importance in the hospitals of France, whereas a more detailed and practical knowledge of how to handle the effects of trauma on these same anatomic structures was a crying need. By the same token, surgery of the chest and orthopedic and maxillofacial surgery demanded the full attention of those who had previously indulged in these fields as a hobby only, and by the time the armistice was signed the specialist as such had ceased to be a necessary evil and was an indispensable member of the surgical profession in the mind of the public. Financial stringency, professional jealousy and the dislocations in civilian practice that arose out of relocating ex-Army doctors, as well as the postwar neurosis that affected to varying degrees almost all who were intimately associated with the armed forces, led to the temporary development, however, of what might be called an antispecialist reaction in the profession itself. This was most noticeable among the staffs of large municipal hospitals and the ranks of the general practitioners. Rather than countenance what was believed by many to be, and what latterly in some cases actually was, an infringement of their surgical rights, these surgeons leaned over backward. In their zeal they attempted to carry on the prewar tradition of being general specialists, and to deal with certain surgical problems that were beyond their mental and technical abilities. It was at this time — perhaps twenty to twenty-five years ago — that the antithesis of the definition of a specialist was most aptly applicable to these general surgeons and the few remaining general practitioners. They were indeed men who knew less and less about more and more.

The Army and Navy, just as they do today, also encouraged general specialism. World War I did not last long enough for them to learn permanently the lesson that armed combat forced them to take cognizance of just before the armistice. Despite the then proved value of specialist consultants and hospitals staffed for and limited to the care of one specialty, it is now apparent that that knowledge has been thrown aside. The old system, whereby the officer-of-the-day who, though trained as an allergist or ophthalmologist, must nevertheless operate on any patient with an acute appendix who is admitted to the hospital at night during his tour of duty, is still in use in this present emergency. To be sure, one general surgeon in every large service hospital may be assigned as a specialist or vice versa, but the fundamental concept in both the Army and Navy men today apparently is still that which visualizes the general surgeon as a general specialist. The armed services appear to ignore the fact that the public has learned by experience that this is a fallacy.

In so far as neurosurgery was concerned, the group with such ideas was aided and abetted by most of the specialists in this field, who for many years after the close of the war, and despite the experience they had had therein, still regarded neurosurgery as the surgery of tumors of the central nervous system. They not only permitted but encouraged the general surgeon to care for the traumatic aspects of this specialty, and found partial justification for this attitude in the large numbers of such cases and the small numbers of neurosurgeons.

Today everything has changed for the better in the profession. By and large, there is a healthy understanding and co-operation between the general surgeon and the specialist. The system of closed-staff hospitals, backed as it is by the American Medical Association, the American College of Surgeons, the American Hospital Association and national nurses' organizations, effectively controls the caliber of the surgery done in the community served. Those who practice surgery are expected by the public to attempt only such surgery as their knowledge and ability permit. Opportunity for adequate postgraduate training is provided for all who can profit by it. Educational programs are constantly provided and the limitations of the general and special surgical procedures are taught to all who will learn. Thus the general surgeon has "policed himself."

What of the specialist? He, too, has set up a method for "policing himself" in his own activities. Boards of certification have been created, methods of examination worked out, and lists of accredited specialists made available to the public. These are all excellent and indispensable steps in improving the care of the public by the profession. Their importance cannot be overemphasized. There are, however, still lacking certain more fundamental steps, that must be taken before the full benefit of the tremendous amount of medical knowledge at present available to the profession can reach the patient. These have to do with the teaching of the medical student. Because no one human brain can possibly hold all this information, and because the student of today is the doctor of tomorrow, the student ought, above all else,

to leave medical school with a clear idea of his own intellectual lack and of where he can supplement it. He and the profession must learn that, from the point of view of actual use, the term "general surgeon" implies ignorance of the specialties, just as the term "specialist" implies ignorance of certain data that are made use of every day by the general man. Neither is capable of doing all things and simultaneously doing any one of them well. A general specialist is a paradox, and a dangerous one at that. So, too, is the specialist who cannot see beyond the walls of his own office. Any necessary specialization of general surgery must be duplicated by the necessary universality of the specialties. Failure to teach this in the schools and inability on the part of the profession to recognize its practical application to everyday practice are holding back the development of both specialist and general man.

As I have said, many general surgeons and practitioners and a disgracefully large number of neurosurgeons still believe that the real mission of the neurosurgeon is to deal with tumors and pain affecting the central nervous system. They will concede that the nervous system is heir to many other surgical ills, but these are regarded, on the one hand, as being too broad in scope for the specialist to deal with, and on the other, as being something to occupy an idle moment with when the neurosurgeon has no tumors or physiologic mysteries to cope with. It is not surprising that this attitude should persist. In my opinion, the educational policies of our medical schools foster it. Because of the tremendous increase in the amount of information that must be taught in four years, there is not time to teach many of the specialties adequately. Such a specialty as neurosurgery, therefore, is taught by the professor of general surgery, or else a few hours of lectures where days should be available are grudgingly granted the neurosurgeon for what use he can make of them. No attention is paid and very likely no knowledge is had of the ramifications of this specialty into almost all the other fields of surgery.

For example, the tremendous number and unjustifiably high mortality of craniocerebral injuries have been matters of common knowledge for years. As recently as the middle of October, 1942, the Mocks stated in the *Journal of the American Medical Association*:

> Facts collected from various sources warrant a conservative estimate of 600,000 serious head injuries . . . as the annual incidence of this type of trauma. With average mortality rates of 10 per cent for serious head injuries without skull fractures and an average death rate of 30 per cent for proved skull fractures, it becomes apparent that 100,000 of our friends, neighbors and relatives are being killed — nearly 300 people each day — by brain injuries.

It is obviously impossible for the neurosurgical specialist to care for all these injured. The majority must be cared for by the general surgeon according to instruction supplied by the specialist, yet no practical effort is made to render these data available to the student, and almost none to furnish them to the house officer, who appears later among the public as a so-called "well-trained" general surgeon. Also let not the neurosurgeon who advocates, as an important part of his special training, giving two years to the study of the cellular pathology of cerebral tumors forget that it took Harvey Cushing thirty-one years to collect 2000 cases of brain tumor. Three hundred times that many brain injuries occur in the United States in one year of peace alone, and fifty times that many patients with brain injuries die as the result of them in the same period. From the viewpoint of the public, of what avail is it to teach a medical student how to deal with a cyst of the pancreas, an adrenal tumor or an internal concealed hernia, or a neurosurgical resident how to differentiate an astrocytoma and an astroblastoma, if neither is taught any of the special methods that will permit him later to reduce this tremendous number of deaths? Can a more striking example of the need for co-operation between general surgeon and specialist be instanced? Is this not the very essence of the universality of a specialty? So too, what of the specialist who receives his neurosurgical training in the leisurely field of tumor surgery, only to find that in practice he must make up his mind at once, sacrifice technical meticulousness for lifesaving speed, and learn through bitter experience that life is indeed short and decision certainly difficult? It must be apparent that in this most important field of medical education and public relations the specialty of neurosurgery has a considerable universality.

Let me give you further less striking but quite as important examples. To continue with injuries: Spinal cord injuries — not so frequent as craniocerebral injuries but more disabling — have resisted successful treatment by general surgeons and neurosurgeons for years. Patients lived in the misery of a constantly wet bed, bedsores, bouts of pyelitis and adduction and flexion contractions of the legs, only to die eventually from sepsis. By invading the field of another specialty — that of genitourinary surgery — and enlisting the help of the physiologist, a method of tidal drainage of the bladder was devised whereby these patients could

be kept dry. Coincidentally, bedsores either did not develop or healed promptly when they did, contractures could be successfully dealt with by operation or splinting under the direction of the orthopedic surgeon, pyelitis disappeared, and major genitourinary sepsis was reduced from 72 to 16 per cent, with a corresponding lowering of the mortality.

Pain in the face is a common symptom. If it comes as lancinating attacks limited to one side of the face and can be constantly reproduced by stimulation of one so-called "trigger zone," the patient is suffering from *tic douloureux* or trigeminal neuralgia. This is strictly a neurosurgical problem. It can be dealt with only by appropriate denervation. Nevertheless, all neurosurgeons will testify that most sufferers from this terrible disease have had many or all their teeth pulled out, at least one antrum of Highmore opened, and other nasal operations galore performed by a dentist or rhinologist before getting to the neurosurgeon. Here the dentist and rhinologist should recognize their own deficiencies and make use of the specialist. On the other hand, the neurosurgeon must not forget his own restricted knowledge when trying to deal with patients who have equally severe but less typical facial pain. Pulp stones, malocclusion and apical infections all are frequent causes of this pain, and all are familiar to the dentist and completely unfamiliar to the neurosurgeon. So, too, affections of the sphenopalatine ganglion, hypertrophied turbinates, a deviated nasal septum, shingles and degenerative changes of the basal ganglia associated with cerebral arteriosclerosis can and often do cause facial pain that mimics closely the classic symptoms of trigeminal neuralgia. Denervation of the face in such cases gives no relief of symptoms. Although the former are old stories to the rhinologist and the latter the same to the general medical man, the neurosurgeon must admit ignorance of their characteristics, diagnosis and treatment except in their most superficial aspects.

Ménière's syndrome or disease, to use the familiar term, is first seen by the otologist. At that time the differential diagnosis includes a number of possibilities. Among the common causes of the syndrome may be an eardrum that needs splinting, a blocked eustachian tube, infectious or other forms of acute labyrinthitis and a tumor of the cerebellopontine angle. What more perfect example of the need for co-operative diagnosis and therapy between specialists could be cited, increased as it may be by the possible need for the services of the allergist, the biochemist and the ophthalmologist? Yet such co-operation cannot even be begun until each doctor concerned recognizes his own intellectual and technical limitations and turns for help to the others when he has reached these limits. The universality of such specialization pays high dividends in grateful and relieved patients, whereas an attempt to generalize a specialty or specialize a general problem leads to nothing but grief for all concerned.

Appropriate cases could be multiplied many times. Headaches, the bane of every professional man's existence, tax the powers of every branch of medicine and surgery, from the gynecologist and endocrinologist to the neurosurgeon and psychiatrist. Low-back pain and the problem of ruptured intervertebral disks have taught the orthopedist that "radiculitis" is more than a fancy word, and the neurosurgeon that some knowledge of bodily mechanics is essential to the proper examination of a back. Brain abscesses and their relation to ear disease make a team of the otologist and the neurosurgeon. The dermatologist who must deal with the distressing symptoms of hyperhydrosis, the obstetrician and pediatrician with their problem of craniocerebral injury to the newborn and the electrophysicist with his unsung contribution to the study of epilepsy are other examples of the need for co-operation between doctors.

Industry has an interest in this. It is probably correct to say that the late effects of injuries to the head and back constitute one of the most difficult problems of industry, and one that is yet unsolved. A study of the records of any impartial examiner — for the Massachusetts Industrial Accident Board, for example — indicates that the chief reason for this is that the claimant, the insurance company and industry itself have for years demanded a definite diagnosis at a minimal cost at the earliest possible moment after the receipt of the injury. The effect of this has been to limit early hospitalization and adequate consultation. It has forced the doctor to make a diagnosis without adequate facts or study. This in turn has led the claimant to become suspicious of the profession and unco-operative with those who may actually have his best interests at heart. The patient turns toward the untrained overworked surgeon, medical man or general practitioner, who has neither the time nor the financial or intellectual assets to have investigations carried out along specialist lines, but who continues to be employed because he is known to be sympathetic with the patient. He sticks to his diagnosis right or wrong, and is often forced to perform underpaid work badly for lack of anything better to do. The crying need in the solution of these difficulties is not to take the patient away from his

doctor, but rather to make it easy for both to have the courage to recognize that the case calls for the use of other professional brains. Only in this way will claimants, insurers and insured get the most benefit from the universality that is inherent in all specialties and particularly in neurosurgery.

I have offered nothing but destructive criticism. That the specialties in general and neurosurgery in particular have a universality cannot be denied, but this is, I fear, not well recognized. What can be done to correct this lack? No move in that direction will be successful until the doctor is taught while still a medical student not to say, "How much I know!" but rather, "How much I *don't* know!" With that concept firmly implanted in his mind and in the minds of his teachers, he and they will see to it that he has a broad general training during his medical-school and hospital years. Part of that training will consist in impressing him with the need and value of tapping other peoples' brains, and with the realization that if he would increase his special knowledge, that increase can come only at the expense of his general information. Specialists must not even be formed in embryo in the medical school. I do not mean that students should not be taught by specialists, but that this teaching must be from the point of view of the general applicability of the specialty. Most important of all, when a specialty is taught by a general surgeon or physician, this must be done from the point of view of the special applicability of the general problem.

Such teaching can have no effect for some years, however fundamental, necessary and overdue it may be. What can we do today? First and foremost we should concentrate our postgraduate education not on teaching new facts to the profession, but rather on impressing them with how many of the old facts they do not know or have forgotten. They will soon find how much happier they are when they learn to say to a patient,"I don't know but will find out," rather than "I don't know, but no one else does either, so it's no use consulting other physicians." As another part of an all-over effort to instrument this universality of the specialties, certifying boards should emphasize the important general aspects of the specialty, minimize the highly technical and special knowledge that is at present rather overvalued, and see to it that the candidate knows what he does not know and understands how to get that knowledge from others who do. Finally, let the specialist himself beware of becoming so superspecialized that he loses touch with reality and becomes a drag on the wheels of progress, instead of acting as a spur to the general surgeon, medical man and practitioner in their attempts to improve their care of the public. Only in this way will the foundations of the practice and the art of medicine be built up into a structure that is free from weaknesses and strong enough to last forever.

SINGLE TRUE CYSTS OF THE SPLEEN*

Reports of Three Cases

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BOSTON

THE rarity of splenic cysts is attested by the fact that up to February, 1941, McClure and Altemeier[1] were able to find only 148 cases of all types reported in the literature. Denneen[2] mentions that at Bellevue Hospital from 1904 to 1940 only 8 cases were revealed in the records of the Pathology Department.

The occurrence of various types of cysts in the spleen has led to the proposal of several classifications of these tumors that seem to be unnecessarily complicated and unimportant. Of these, that recently proposed by McClure and Altemeier[1] appears to be the best. All cysts of the spleen may be grouped under two headings, the true and the false, depending on whether or not they are lined by a specific secreting membrane.

True cysts are much less frequent in occurrence than are the false cysts. Of the 137 cases collected from the literature by Fowler,[3] 21 per cent were of this variety. The 3 cases reported here were large unilocular true cysts, each with a specific lining membrane.

DIAGNOSIS

Because cysts of the spleen are encountered so rarely, the impression exists that the diagnosis is difficult. This is no doubt the case when they are small. Large cysts, however, present a clinical picture which is so characteristic that the diagnosis can be readily made. The subjective symptoms, excepting for the fact that a tumor is noticed, are so negligible that the clinical history is of little value. A dull dragging pain or discomfort in the left upper quadrant of the abdomen may be complained of. From the diagnostic standpoint the greatest help is to be obtained from the physical examination and the roentgenological findings. The significant data in the 3 cases subsequently reported are listed in Table 1.

Physical Examination

There is always a large abdominal tumor that on careful palpation is found to occupy the left upper quadrant of the abdomen, whence it extends into the lower abdomen and toward the right side to an extent depending on its size. The left costal margin is usually pushed outward by the tumor, which always extends beneath it. This does not as a rule occur in pancreatic cysts, and rarely occurs in ovarian ones. The lower border of the tumor even when very large does not occupy the pelvis in the way an ovarian cyst does. That the tumor is cystic can often be determined by the sensation of resiliency imparted on bimanual palpation. A definite fluid wave can usually be detected in large cysts. This was so in the largest two of the three tumors in this series.

X-Ray Examination

When all the evidence is assembled, the roentgenologic examination in cases of large splenic cyst is so typical that it may for all practical purposes be considered diagnostic. The left side of the diaphragm is high, and under the fluoroscope its motion is impaired. A plain abdominal plate shows a large, soft-tissue mass arising in the left upper quadrant. Hampton[4] has called attention to the fact that the lower pole of this shadow in cases of splenic cyst has a somewhat angular, almost pointed contour that extends downward and to the right into the pelvis. This observation is based on the appearance of the shadow cast by the tumor in the 3 cases reported here, and depends on the fact that in all these cases the cyst developed in the upper pole of the spleen, leaving a small, intact, triangular lower pole at the lower extremity of the tumor. If the cyst should happen to develop in the lower pole, this finding would doubtless not occur. After a barium meal the stomach is found to be pushed to the right, and if the tumor is a large one it is pushed backward as well. The colon, especially the transverse, splenic flexure and descending portions, is found displaced downward and to the right. The left kidney as visualized by intravenous pyelography is shown to be pushed downward by the tumor. The contour of the kidney pelvis is usually not altered.

In any case of large abdominal tumor that appears to arise from the left upper quadrant of the abdomen and feels cystic on palpation, the above-described x-ray findings are practically diagnostic of cyst of the spleen. Some of these are well demonstrated in the roentgen-ray films of Case 1, which are reproduced in Figures 1, 2 and 3.

*Prepared for presentation at the canceled 1942 meeting of the New England Surgical Society.

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Treatment

In the present state of surgical knowledge and experience, it is useless to describe the obsolete operations of marsupialization, incision and drainage, or local excision or enucleation of these cysts. Splenectomy is by far the simplest and safest procedure and should be adopted in all cases.

All recent reports agree that splenectomy in these cases is a safe and reasonable procedure, with a mortality of not more than 4 per cent.[3] There is a rapid restoration of the normal relations of the viscera that were displaced by the tumor. The roentgen-ray proof of this is well borne out in Case 1. A plate from this case (Fig. 5) shows that before the patient left the hospital the stomach and colon were back in approximately normal position.

Table 1. *Significant Data in 3 Cases of Large, Single True Cyst of the Spleen.*

Data	Case 1	Case 2	Case 3
Age	19 yr.	23 yr.	8 yr.
Sex	F	F	M
Symptoms:			
Duration of abdominal swelling	2 yr.	9 yr.	10 wk.
Dull pain (in left upper quadrant)	+	0	0
History of trauma	0	0	0
Physical examination:			
Tumor apparently arising in left upper quadrant	+	+	+
Left costal margin pushed outward	+	+	—
Tumor cystic-feeling	+	+	+
Fluid wave detected	+	+	0
X-ray examination:			
High left diaphragm	+	+	+
Limitation of motion of diaphragm	+	+	+
Mass in left upper quadrant	+	+	+
Small triangular lower pole at lower extremity of mass	+	+	+
Stomach displaced to right	+	+	—
Stomach displaced to right and posteriorly	+	—	—
Stomach displaced to right and downward	—	+	—
Colon displaced downward and to right	+	+	—
Left kidney displaced downward	+	+	+
Restoration of stomach, colon and left kidney to normal after splenectomy	+	—	—
Pathological examination:			
Size of tumor	45 by 30 by 30 cm.	30 by 30 by 17 cm.	11 by 16 by 17 cm.
Weight of tumor	17.3 kg.	4.7 kg.	?
Nature of fluid contents	Thin, dark-red and hemorrhagic	Thick and brown (3 liters)	Thin, turbid and brown
Nature of cyst:			
Type	Unilocular	Unilocular	Unilocular
Walls trabeculated	0	+	+
Lining membrane	+	+	+
Nature of lining membrane	Thin layer of flattened endothelial-like cells	Thin layer of flattened endothelial cells	Single layer of cuboidal cells
Splenectomy performed	+	+	+
Result	Cured	Cured	Cured

Case Reports

Case 1. L. S., a 19-year-old girl, was admitted to the Massachusetts General Hospital on March 22, 1940, complaining of a gradually enlarging abdomen. Approximately 2½ years before admission she first noted the presence of a steady, dull, somewhat ill-defined aching pain in the left upper quadrant of the abdomen beneath the rib margins. This discomfort continued, and 2 years before entry she noticed a lump in the left upper abdomen in the same vicinity in which the pain was arising. She was otherwise well and led a fairly normal life until 6 months before admission, when she became cognizant that the same quadrant of the abdomen was swelling. It seemed to enlarge to the left and was definitely hard. With this enlargement the patient experienced mild distress in breathing deeply and complained of a sensation of fullness after the ingestion of moderate-sized meals. The constant pain had many superimposed sharp twinges. There was no vomiting, but for several months there had been slight morning nausea. She denied pregnancy and stated that her catamenia had been normal. The last menstrual period occurred 5 days before admission and the one previous to that occurred 3½ weeks before admission, with normal flow and no clots or pain. During her illness there had been no change in weight. She noted an increasing ease of fatigability and, because of the abdominal mass, discomfort while walking.

Figure 1. *Case 1.*
The plain abdominal film shows a large splenic cyst.

Physical examination revealed a healthy-appearing, obese girl. She had a very slight mustache, with stiff but sparse hairs on the chin, hairs on the chest and a masculine distribution of the pubic hair. Examination of the heart and lungs was negative. The blood pressure was 130/100. The abdomen was protuberant and slightly asymmetrical, so that the left upper quadrant bulged slightly more than

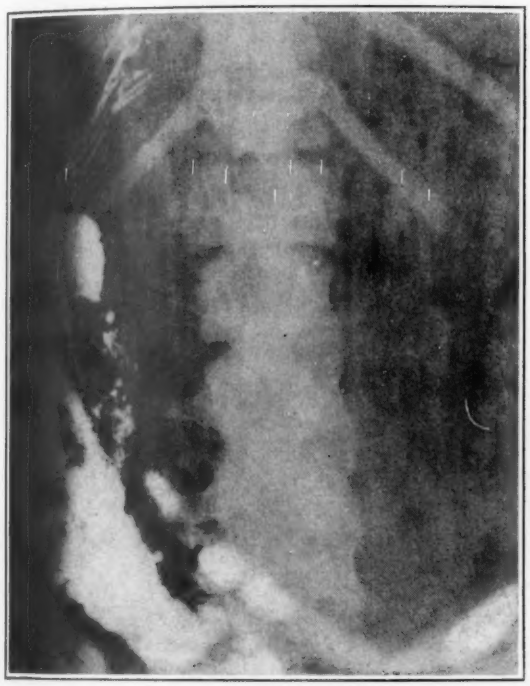

FIGURE 2. *Case 1.*

The film of the upper gastrointestinal tract shows that the stomach and jejunum are pushed to the right side of the abdomen by the cyst.

did the right. On palpation a cystic, smooth, ovoid tumor mass was noted, which transmitted a good fluid wave. There was no shifting dullness in the flanks. The tumor moved slightly on respiration. Pelvic examination showed a slightly enlarged nulliparous cervix.

Examination of the blood showed a red-cell count of 3,700,000, with 75 per cent hemoglobin, and a white-cell count of 12,600, with 75 per cent neutrophils; a smear was essentially normal. The stools were negative for occult blood. A blood Hinton test was negative. The serum nonprotein nitrogen and protein levels were normal. A sugar-tolerance test showed the following findings: fasting, 74 mg. per 100 cc.; 30 minutes, 176 mg.; 1 hour, 167 mg.; 2 hours, 77 mg. Urine examinations showed specific gravities of 1.018 to 1.028 and 0 to ++ tests for albumin, and the sediment contained 5 to 10 white cells per high-power field. A urine culture showed a moderate growth of nonhemolytic streptococci. The vital capacity was 3250 cc. A 17-ketosteroid determination was normal (9 mg. per 100 cc.).

Roentgenograms of the abdomen revealed an unusually large soft-tissue mass completely filling the upper abdomen and extending downward to the level of the lower border of the left sacroiliac joint (Fig. 1). The margins of this mass were smoothly rounded and sharply defined. Intravenous pyelograms showed that the dye appeared promptly on the right side and that the right pelvis and calices were normal. On the left in one of the films there was a small quantity of dye visualized in a region that probably represented the pelvis of a normal left kidney. The calices were incompletely demonstrated. The left kidney was displaced downward. All the visible bones appeared definitely older than indicated by the patient's age. This was particularly true of the lower lumbar vertebras, which showed wavy configurations of their surfaces. All the visible epiphyses were closed. A chest plate revealed a high diaphragm, regular in outline. The lung fields were clear. The heart was normal in size and shape. There was no evidence of metastases. By fluoroscopy the left side of the diaphragm was seen to move poorly, while the right side showed fair motion. A barium meal with fluoroscopic observations showed that the stomach and small intestines were markedly displaced to the right and posteriorly by

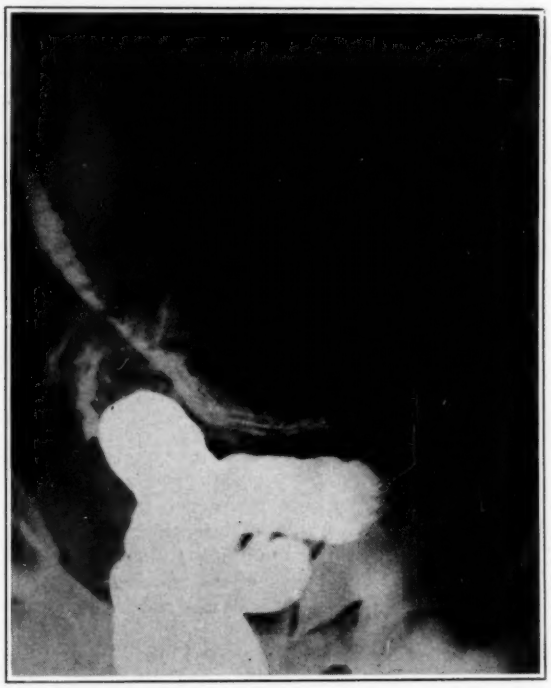

FIGURE 3. *Case 1.*

The barium enema demonstrates that the transverse and descending portions of the colon are pushed downward by the cyst.

the huge mass (Fig. 2). A barium enema revealed that the splenic flexure was markedly displaced downward by the tumor mass, the transverse colon running along the lower edge of the tumor (Fig. 3). The hepatic flexure was not displaced.

On April 5 the patient was operated on. A long, left-rectus, muscle-splitting incision was made, extending from the xiphoid to within 5 cm. of the pubes. The abdomen was opened and the tumor was found to be an immense cyst of the spleen arising from the upper pole. The lower pole was easily identified and extended into the pelvis. The vessels of the splenic pedicle entered the tumor at its lower portion. These were easily ligated

and the lower portion of the spleen was freed. There was a dense adhesion of the cyst to the left lobe of the liver, which had been thinned out over a portion of the tumor, and several other dense adhesions to the peritoneum and diaphragm. The stomach, colon and small intestines were not adherent to it. The kidney had been

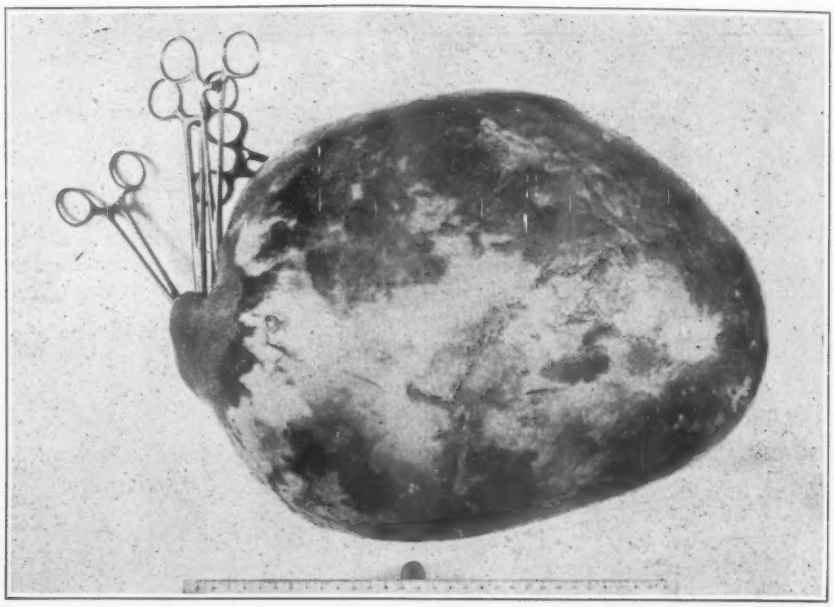

FIGURE 4. *Case 1.*

This is a photograph of the cyst taken soon after removal. Note the lower pole of the spleen, which gave rise to the pointed contour at the lower extremity of the x-ray shadow.

markedly displaced downward by the tumor, the upper end of which occupied the right upper half of the abdomen from front to back. It seemed to contain many areas of necrosis or at least of hemorrhage into its substance. After removal of the tumor without breaking it, many small bleeding points in the undersurface of the diaphragm were tied off and the abdominal wound closed in layers in the usual way.

Pathological examination showed a tremendous, tense, partly red-brown and partly grayish, smooth-walled, ovoid cyst measuring 45 by 30 by 30 cm. and weighing 17.3 kilograms (38 pounds), the upper portion of which was intimately blended with and appeared to arise from the spleen, measuring 8 by 5 by 5 cm., which was splayed out over the cyst (Fig. 4). There were a few fibrous shreds scattered over the surface of the cyst and also a few small, whitish areas. On palpation a fluid wave was present. The cyst was found to consist of a single large cavity filled with dark-red hemorrhagic fluid and having a tough and apparently fibrous wall. It was lined by a thin, flattened, endothelial-like membrane and was completely encapsulated by relatively dense connective tissue. No definite indication of the origin of the lesion was apparent. A diagnosis of splenic cyst, unclassified, was made.

The patient stood the operation well and her convalescence, though briefly complicated by collapse of the left lower lobe, was rapid and essentially uneventful. A postoperative x-ray film (Fig. 5) showed that the stomach and colon had returned approximately to their normal positions. She was discharged on the 17th postoperative day.

CASE 2. M. S., a 23-year-old woman, was admitted to the Baker Memorial on August 2, 1932, because of a large abdominal mass. Nine years previously when she was undergoing a routine physical examination a large, firm, solid mass had been found in the left upper quadrant of the abdomen. She was told at this time that the mass was a large spleen and would cause her no trouble. She was thoroughly studied by x-ray and blood studies were done, and a diagnosis of splenomegaly was made. The mass continued to enlarge and doubled its size in 6 years, but there was still no discomfort from it. It filled the entire abdomen, but was larger on the left than on the right. Although the patient had been barred from all athletics during her college course, she had not considered herself handicapped by the tumor. She had never been jaundiced. There had been no evidence of any ovarian disorder; her periods had been as regular as usual, with no metrorrhagia and no menorrhagia. She had bled rather freely after a tonsillectomy 6 years previously and at another time after a tooth extraction. The appetite was good. The bowels moved freely once a day without catharsis and the patient had passed no bloody or tarry stools. She had no urinary symptoms.

Physical examination revealed a well-developed and well-nourished young woman in no distress. The heart was normal. The blood pressure was 118/76. In the left upper quadrant of the abdomen there was a deformity of the rib margins due to pressure from within. A nontender, firm cystic mass could be felt in this region. There was definite elasticity and fluctuation. There were

no other masses in the abdomen. The cyst extended well out into the flank.

X-ray examination showed a huge, soft-tissue tumor occupying the upper two thirds of the left side of the abdomen. It displaced upward the left side of the diaphragm, which was limited in excursion but smooth in outline.

FIGURE 5. *Case 1.*

The postoperative film of the gastrointestinal tract shows that the stomach and jejunum have been restored to normal position.

Fluoroscopic examination of the chest showed no other variations from normal. What appeared to be the kidney outlines were unusually low in position. The edge of the liver also appeared low. Small collections of gas were seen in the bowel, and these gas bubbles were markedly displaced downward and to the right. What probably represented a gas-filled stomach lay in the right lower quadrant. The lower edge of the tumor was sharp in outline and descended below the crest of the ilium (Fig. 6). The right edge was 4 cm. lateral to the vertebras, and within the right edge of the tumor one small area of calcification was seen. There was no evidence of erosion of the vertebras or ribs. There was some kyphosis at the dorsolumbar junction and upward displacement of the ribs.

On August 4 the patient was operated on. A left paramedian incision was made and a large tumor was seen beneath it. This was found to be a large cyst of the spleen that had thinned out the whole spleen except for an area 5 cm. in width and 8 cm. in length at the lower pole. The rest of the spleen was spread out over the anterior and posterior surfaces of the tumor. The tumor was adherent posteriorly and especially to the diaphragm. The pedicle entered the lower pole of the spleen. This was tied off, the adhesions were separated, and the whole tumor was turned out of the abdominal cavity. There was comparatively little bleeding. All denuded areas were covered with peritoneum and the wound was closed without drainage. The appendix was removed and the stump buried.

Pathological examination showed a tumor measuring 30 by 30 by 17 cm., and weighing 4.7 kilograms (10¼ pounds), covered by splenic tissue, only a 12-by-4-by-2-cm. piece of actual spleen remaining. A large white area 14 cm. in diameter was seen on one surface. The remainder of the surface was deep red. The tumor was fluctuant. It was filled with 3 liters of thick, brown fluid. The walls were trabeculated, whitish and entirely fibrous. The appendix was slightly thickened, with a fecalith 3 mm. in length in the distal portion of the lumen. A diagnosis of cyst of the spleen and healed appendicitis was made. The wall of the cyst was made up of dense bands of fibrous tissue. An inner lining could not be made out, possibly because of long fixation before opening. A thin layer of flattened endothelial cells was vaguely outlined.

FIGURE 6. *Case 2.*

This plain abdominal film clearly illustrates the pointed contour at the lower extremity of the shadow.

Following operation the patient made an uneventful recovery and was discharged on the 15th postoperative day.

CASE 3. R. U., an 8-year-old boy, was admitted to the Baker Memorial on February 2, 1931, because of swelling of the left side. Ten weeks previously a swelling had been noted on the left side below the rib margin. From then until admission it seemed to be getting gradually larger, although it had been painless and there had been no associated symptoms other than some loss of weight.

The patient's appetite had always been poor and he was extremely constipated, requiring a laxative about once a week. There were no genitourinary symptoms.

Physical examination was negative except for a large, rounded elastic tumor palpable in the left upper quadrant.

X-ray examination of the chest revealed the diaphragm high on the left side and slightly limited in excursion. It was normal in outline and moved well on the right. Examination of the genitourinary tract showed massive soft-tissue dullness in the left upper quadrant, apparently displacing the left kidney downward and extending to the level of the fourth lumbar vertebra. The mass was roughly triangular and in the anterior-lateral position. The upper pole of the left kidney was at the level of the second lumbar vertebra and the lower pole opposite the fourth lumbar vertebra, but other than this the left kidney was not abnormal. X-ray examination after the injection of Uroselectan failed to give any additional information.

On February 5 an operation was performed. A vertical incision was made extending from the ensiform nearly to the pubes. There was a large cyst of the spleen. The vessels on the inner side of the tumor were clamped and cut, and the adhesions of the diaphragm and undersurface of the tumor freed by blunt dissection or cutting. After the tumor had been freed it was found to be so large that it was almost impossible to deliver it, as it seemed to be wedged tightly between the chest wall and the vertebral column. This was accomplished, however, with little bleeding. The denuded areas were covered with peritoneum except those on the diaphragm where the adhesions had been cut, and the wound was closed without drainage. The liver was normal in size and color. There were no enlarged lymph nodes and there was nothing suggesting malignant disease.

Pathological examination showed a purplish-red cystic tumor measuring 11 by 16 by 17 cm., with a smooth surface and resembling the spleen. The spleen itself was compressed and formed a large portion of the wall of the cyst. At the poles of the cystic mass the splenic tissue was more abundant. For about half its circumference where it was uncovered by the spleen the wall was thin and fibrous. The cyst was filled with thin, turbid, brown fluid. The inner surface was smooth and in places showed coarse trabeculations. On microscopic examination it was found to be lined by a single layer of cuboidal cells. The adjacent walls were composed of degenerate fibrous tissue. The sinuses of the spleen were dilated, the lymph follicles were diminished, and the reticulum was prominent. The gross and microscopic appearances were suggestive of an origin from a lymph sinus. A diagnosis of simple cyst was made.

The postoperative course was uneventful and the patient was discharged on the 16th postoperative day.

Summary and Conclusions

The findings of physical examination of the abdomen taken with the characteristic x-ray appearances should enable one to make a diagnosis in cases of large true cyst of the spleen.

Following splenectomy the abnormally displaced stomach, colon and left kidney assume their normal positions.

Three additional cases of large single true cyst of the spleen are reported.

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ROENTGENOGRAPHIC SURVEYS FOR TUBERCULOSIS IN MASSACHUSETTS AND THEIR IMPORTANCE TO THE PHYSICIAN

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BOSTON

THE war has brought some danger of a rise in the prevalence of tuberculosis but it has also brought a tuberculosis case-finding project of far greater magnitude than any previously contemplated. The United States Army, aided at the beginning by the Massachusetts Department of Public Health, is engaged in making 4-by-5-inch stereoscopic photofluorograms of the chests of all men inducted under the Selective Service Act or volunteering for enlistment. These films are interpreted before the completion of the physical examination. In addition, the United States Navy is making routine 35-mm. photofluorograms of enlisted men at naval training stations. More than 2000 men have been rejected for military service in Massachusetts by the Army alone because of tuberculosis or suspected tuberculosis.

The names and addresses of Army rejectees are forwarded from the examining station to the Department of Public Health. The state district health officer, working through the local board of health, later attempts to secure answers to the following questions on each case:

> Has the patient been x-rayed again? If so, by whom?
>
> State the findings.
>
> Was the diagnosis of tuberculosis confirmed? If so, has the case been reported?
>
> What further study or treatment has been recommended? Is this being carried out?
>
> If the diagnosis was confirmed, give the number of household contacts, the number who have been x-rayed and the names of any found to have tuberculosis.

In the field of industry routine chest x-ray films are also coming into frequent use. Several large plants in Massachusetts employing thousands of men have recently made them a part of every preemployment examination, and the opportunity of a survey of all workers will soon be offered to many other plants if present plans are carried through. Many colleges likewise require x-ray examination of students. Cases discovered through industrial surveys conducted by the Department of Public Health are handled as follows: the individual is told that he or she has a chest condition needing treatment or further study and is asked to designate a physician to whom the roentgenographic report can be sent. Only if the patient states that he has no physician, cannot afford one or has no intention of going to one is the alternative of attendance at a tuberculosis clinic suggested.

Physicians may, therefore, expect to see numbers of men and women who have been told that they have tuberculosis and referred to their own doctors for advice, treatment or further study. Cases thus referred can be classified in several groups. The simplest is the obvious case of *active tuberculosis* needing sanatorium treatment and, possibly, collapse therapy. Repetition of the x-ray examination is often unnecessary, especially if partial confirmation is obtainable by physical examination. There are three steps to be taken: reporting the case, arranging for admission to a sanatorium and examining by x-ray all household contacts. It is sometimes assumed that because a state clinic has made the x-ray examination these cases are already reported, but this is not correct; reporting is left to the physician. Diagnosing and reporting tuberculosis on the basis of x-ray evidence alone sometimes results in errors.

A second group has been classified on the basis of x-ray findings as *tuberculosis suspects*. This generally means that the roentgenologist has seen a small hazy or infiltrative shadow but is not sure enough of its presence or significance to label it pulmonary tuberculosis. These patients invariably should have another film taken. If the technic is better, sometimes this alone decides the question; or the lesion previously seen may have disappeared, indicating that it was an acute pneumonitis. More often, however, the second film, particularly if taken after a short interval, merely provides a basis for comparison with subsequent ones, since the original survey film is not usually available for this purpose. Symptoms and physical signs are unlikely to aid in the diagnosis, since they are not usually elicited in such early cases. Changes in the differential leukocyte count, an afternoon fever and an elevated sedimentation rate may have confirmatory value, but one should not wait for their appearance to institute treatment; furthermore, they are not specific for tuberculosis. Once in a while tubercle bacilli are found in the sputum or gastric contents of a suspect by culture or guinea-pig inoculation, but this occurs too

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seldom to be of great assistance. Serial roentgenograms are the only reliable test. Their frequency depends on the patient's age, the nature of the lesion and the opinion of the roentgenologist. In young adults, they may be spaced from one to four months apart at first. Persistence of the lesion unchanged may indicate stability or may be a sufficient reason to institute treatment, depending on the radiologic appearance. Evidence of gradual regression or fibrosis is proof of recent activity and hence may call for even more frequent observation than a stable lesion.

Many of these remarks apply with equal force to the third group, called *inactive or healed tuberculosis*. It is advisable to obtain a roentgenographic record of the cases classified as healed, and if there is any doubt about their status, especially if the patients are young and the lesions are of more than minimal extent, they should be kept under periodic x-ray observation until the physician is satisfied that they are inactive. Occasional misunderstandings arise through the confusion of the stage of disease with the question of activity. A classification of minimal, moderately advanced or advanced refers solely to the extent of involvement, not to the activity of disease; "minimal active tuberculosis" and "far-advanced inactive tuberculosis" are correct expressions. The standard basis for classification both of extent of disease and of clinical status is that of the National Tuberculosis Association. Patients are divided according to clinical status into five groups — apparently cured, arrested, apparently arrested, inactive and active. No such exact classification can be made or is attempted from a single observation. There is even a large error in classifying cases simply as active or inactive on the basis of one x-ray film without the assistance of clinical study, although if cavities are visualized there is no question.

Primary phase tuberculosis is a diagnosis frequently made but seldom of any clinical significance in adults. It is rarely seen in an active stage; usually it is manifested by one or more calcified parenchymal nodes or tracheobronchial nodes or both, constituting a calcified primary complex. The Army rejects these men if the lesions exceed certain limits of size or number. The Department of Public Health does not refer to such cases at all when they are encountered in industrial surveys, unless the appearance of the lesion is most unusual. Inactive primary tuberculosis is not reportable and does not require treatment. If the parenchymal calcifications are multiple and associated with some fibrosis, it may be impossible to distinguish them from healed reinfection-type pulmonary tuberculosis unless the whole course of their development has been watched. Active primary tuberculosis, of course, is reportable and requires attention. It often cannot be differentiated from reinfection-type tuberculosis.

Pleurisy with effusion is rarely found in these surveys. Evidence of old pleurisy, such as obliterated costophrenic angles, is of common occurrence, but requires no attention unless the attack occurred within the past five years.

A great many *nontuberculous lesions* are found, some of which are unavoidably mistaken for tuberculosis. Acute respiratory infections, including the so-called "virus pneumonias," may be encountered in ambulant persons who think they have an ordinary cold. If the true nature of these is suspected, re-examination in four to six weeks is advised; the shadow will then have disappeared. Bronchiectasis, atelectasis, suppurative lung abscess, lymphoma, sarcoid, cystic disease of the lung and primary or metastatic carcinoma of the lung are occasionally seen. Emphysema and generalized pulmonary fibrosis, idiopathic or secondary to some other condition, may be recognized. Spontaneous pneumothorax is rarely discovered.

Cardiac lesions are often found in persons who did not know of their existence, sometimes even with signs of pulmonary congestion. Rheumatic, hypertensive, syphilitic and occasionally congenital types of heart disease may be encountered. Diaphragmatic hernias, situs inversus and spine or rib anomalies are seen.

* * *

Physicians in all parts of the State have diagnostic x-ray service available for patients who cannot afford to go to a roentgenologist. All the public sanatoriums maintain outpatient departments, most of them have consultation clinics, and the large cities have their own dispensaries with x-ray facilities. Reports are made to the referring physicians. Sputum examinations are performed without charge by the Bacteriological Laboratory at the State House and by the health-department laboratories in Boston and other large cities. The search for acid-fast bacilli in a stained smear, incidentally, is coming to be regarded as a rather crude test; many cases are positive only on a concentration test, guinea-pig inoculation or culture. The last-named modification as now carried out is an inexpensive, highly sensitive procedure that is being used more widely than before. It reveals the organism in so many patients who were not formerly suspected of having active disease that ideas regarding the significance and frequency of positive sputums have had to be somewhat modified. When smears are negative in a case with clinical evidence of activity, the more sensitive methods of examination should be tried. Patients who do not expectorate may show tubercle bacilli of gastric lavage.

It should be remembered that tuberculosis is a disease of adults and is seldom found in children after infancy and before adolescence; that its prevalence tends to increase with age from adolescence on; that the frequency of inactive disease also increases with age; that the majority of reinfection-type lesions found in young persons are unstable; and that many lesions in older persons are a greater source of danger to their associates than to themselves. These epidemiologic points are given detailed consideration by Chadwick and Pope[1] in their monograph on the public-health aspects of tuberculosis.

A tuberculosis specialist in Boston has repeatedly stated that physicians are not interested in tuberculosis because the State has so largely taken over its treatment. There is truth in this assertion, as shown by the fact that the Section on Tuberculosis of the Massachusetts Medical Society was discontinued for lack of attendance at the annual meeting. Three factors in tuberculosis — its well-known association with poverty, its chronicity and its contagiousness — have been responsible for its control having been largely assumed by public and voluntary agencies. The majority of patients can neither support their families nor pay for treatment during the necessarily long periods of hospitalization. Public ownership and operation of sanatoriums and clinics were inevitable and need no defense at this late date, for they have unquestionably been the most effective means of making adequate treatment available to every patient. However, this has taken away from the majority of physicians the opportunity of seeing the various features and manifestations of tuberculosis. Yet, private practitioners must make the initial diagnosis in most cases. It is highly important that this diagnosis be made as early as possible, for two obvious reasons: to institute treatment before it is too late, and to prevent the spread of the disease to others. In this respect the program has failed. Sanatorium records show that the proportion of far-advanced cases admitted for the first time has not declined and that the proportion of minimal cases has not risen, in spite of the wider use of x-ray films. X-ray study is finding early cases, but the numbers thus found are still too small to influence greatly the stage of disease on admission. Surveys cannot reach everyone; the public must be educated to consult a physician earlier, and the physician must be on the alert.

There is still aversion on the part of some doctors to reporting cases to the local board of health, because they think it will do no good, will result in unwarranted interference with the patient's private affairs or will prove embarrassing to him. Others neglect to report cases because of indifference or pressure of work. Many cases come to the attention of health departments only at the time of death.

If the value of reporting can be convincingly shown, physicians will not fail to report their cases at the time of diagnosis as required by law. The responsibilities that the local board of health assumes, or should assume, when a case is reported include the following: making arrangements for admission to a sanatorium, if necessary; instructing the family in the precautions to be observed while the patient is at home; seeing to it that all household contacts are x-rayed and that those requiring further periodic examinations receive them; helping the family to obtain public assistance, when needed; and keeping in touch with the patient after his return from the sanatorium, in order to assist with any new problems that may arise.

Few physicians have the time or inclination to bother with these details, yet they are important. The board-of-health nurse should be given freedom to work with the families of tuberculous patients, and this assistance is almost always welcomed when the family understands its purpose and has become acquainted with the nurse. If, however, at the time of report the physician indicates that he wishes to assume all the responsibilities mentioned above, the local board is willing to have him do so. It was the opinion of the late Dr. Frederick T. Lord,[2] who served as president of the Massachusetts Tuberculosis League during the last few years of his life, that more aggressive measures should be taken by boards of health to enforce the laws and regulations for case reporting, case supervision and examination of contacts.

* * *

There is great satisfaction to the physician, and great benefit to the community, in having made an early diagnosis and instituted treatment in a case of tuberculosis, and having perhaps found a second case among the family contacts. It is not known just how many cases are thus prevented, but unfortunately there are numerous examples of fatal tuberculous disease in infants exposed to parents or others with open tuberculosis. Case-finding surveys will initiate the attack on unsuspected tuberculosis, but the physician must carry it through.

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MEDICAL PROGRESS

SKIN CHANGES OF NUTRITIONAL ORIGIN (Concluded)*

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PITYRIASIS RUBRA PILARIS

PITYRIASIS rubra pilaris is a chronic benign dermatosis with a varied course.[83] It may show a familial trend.[84] The basic lesion is an acuminate, horny papule involving the follicular orifice. The papules always remain discrete, giving the skin the feel of a nutmeg-grater.[83] The presence of these lesions on the dorsum of the fingers is especially characteristic. Dryness of the skin, with a tendency to fissuring and, when severe, to desquamation, are present. The palms, soles, elbows and knees are horny and thickened and yellowish. The face looks waxy. The skin thickens and is inelastic. Most cases are seen in young adults, but the condition may occur at almost any age. There are no constitutional symptoms and the general health is unimpaired.[83-85] "The essential pathologic process of pityriasis rubra pilaris is follicular hyperkeratosis."[83]

The resemblance of this dermatologic disorder to the skin lesions of avitaminosis A was early commented on by Pettler,[86] and Sutton and Sutton.[85] The last-named authors state, "The similarity of the lesions [of pityriasis rubra pilaris] with those of avitaminosis A is noteworthy, and we add here that these conditions are indistinguishable as judged by the literature, photographs and photomicrographs."

The important work of Brunsting and Sheard[83] has done much to clarify the basic understanding of this disorder and to stimulate a renewed interest in it. They studied 3 patients with pityriasis rubra pilaris and demonstrated that each had impaired dark-adaptation, a finding considered diagnostic of vitamin A deficiency in the absence of organic eye disease. One patient had been subjectively aware of night blindness. Inadequate diet did not appear to be the responsible factor. On massive doses of vitamin A (150,000 international units daily) the impaired dark-adaptation of 2 patients returned to normal in two to four weeks; the third case could not be adequately followed up. One patient manifested a high blood carotene. This suggests that the yellowish color of the skin noted in this disorder is at times due to carotenemia, and that impairment in utilizing carotene may be a basic factor in the pathogenesis. Continued vitamin A therapy for weeks to months resulted in a slow and definite but not complete improvement in the skin lesions. Brunsting and Sheard consider that in part, at least, pityriasis rubra pilaris may be due to a disturbed vitamin A metabolism.

O'Leary[87] believes that there are two types of pityriasis rubra pilaris. The patients in one group have a detectable night blindness and are helped by vitamin A therapy. In the other group evidence of vitamin A deficiency cannot be demonstrated and the skin lesions are not improved by vitamin A therapy. He adds, however, that the patients in the second group may have a deficiency of some other vitamin or combination of vitamins necessary for the utilization of vitamin A that has not yet been recognized. Gross[88, 89] noted improvement in pityriasis rubra pilaris with niacin and with yeast therapy, a point suggesting a more complex deficiency than that of pure avitaminosis A or improvement in liver metabolism of vitamin A. Pettler[86] has reported patients with pityriasis rubra pilaris who responded favorably to vitamin A therapy, as have others.[90, 91]

ICHTHYOSIS

Ichthyosis simplex is a congenital abnormality of cornification of the skin, commonly beginning months to years after birth and characterized by a dry, rough, fissured, scaly skin with diminished sebaceous-gland and sweat-gland activity, which is worse in the winter and improves in summer.[92] It is a not uncommon condition, especially when of mild degree. A hereditary trait is frequently noted. On rare occasions the eyes are involved.[93]

Cod-liver oil has been used empirically in the past for the treatment of ichthyosis. Sulzberger and his co-workers[94] specifically credited the improvement noted in mild ichthyosis that they treat-

The articles in the medical-progress series of 1941 have been published in book form (*Medical Progress Annual*. Volume III. 678 pp. Springfield, Illinois: Charles C Thomas Company, 1942. $5.00).

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ed to the prolonged use of massive doses of vitamin A. Baer and Vogel[95] reported that 3 ichthyotic patients treated with vitamin A manifested improvement in both their skin lesions and dark-adaptation curves. This was proof that varying degrees of night blindness may occur in ichthyotic patients. Vail[93] noted improvement in both corneal and skin lesions of an ichthyotic patient treated with vitamins A and D. None of these papers, however, present the authors' data in detail.

Rapaport, Herman and Lehman[92] reviewed the considerations linking ichthyosis to vitamin A deficiency. These included the following: frequent association in the same patient of both ichthyosis and the follicular keratotic lesions of avitaminosis A; ichthyotic lesions on the legs of patients in published illustrations depicting the skin lesions of vitamin A deficiency; a seasonal fluctuation, with great amelioration or complete return to normalcy during the summer in both ichthyosis and the phrynoderma of vitamin A deficiency (improvement for the latter condition has been explained by the greater vitamin A content of foods during the spring and summer months); a frequent delay in the first appearance of ichthyosis until after weaning; a marked dryness of the skin in both conditions, with deficiency or absence of sweat-gland and sebaceous-gland secretions; a predilection for involvement of the same regions of the skin in both conditions; and similarity in the pathologic histology of the skin in both disorders.

Rapaport and his co-workers made an extended study of 6 patients with ichthyosis. Five who were examined by means of a photometer were found to have impaired dark-adaptation (night blindness). Both the night blindness and the skin lesions responded to vitamin A therapy — the former quite readily, the latter only after prolonged use of large doses. Improvement in the skin was striking but did not reach entire normalcy. A physician-patient who recorded careful observations manifested notable improvement on 60,000 to 100,000 international units of vitamin A daily for two years, the improvement being maintained through two winters. Treatment was then discontinued during four summer months, with recrudescence of the ichthyosis, which again responded favorably when vitamin A therapy was reinstituted. This observation indicates the need for prolonged and continuous vitamin therapy in ichthyosis. Another patient did not respond to the oral administration of vitamin A, but improved considerably with intramuscular injections of 100,000 international units of this vitamin two to three times weekly for several months. The intramuscular preparation contained practically no vitamin D, thus excluding the possibility that the vitamin D present in most fish-liver-oil concentrates was responsible for the favorable response to oral therapy in some patients. This parenteral response suggested defective absorptive of vitamin A from the gastrointestinal tract. However, Rapaport et al. emphasize that there are "many possible disturbances in the chain of vitamin A metabolism, which begins with ingestion at one end and progresses through digestion, absorption, conversion, storage, transportation and so on to finally, at the other end, utilization of the vitamin A by the retina and other epithelial tissues." The mechanism of vitamin A deficiency might function anywhere along this chain, and might even vary from patient to patient. The hereditary mechanism so often present in ichthyosis is explained by Rapaport et al. as possibly one of inheritance of some disorder of vitamin A metabolism rather than one of a direct inheritance of the abnormal skin. In other words, the patient develops ichthyosis because he inherited the inability properly to absorb or metabolize vitamin A.

It should not be overlooked that an ichthyotic-like skin may occur in chronic pellagra. Field and his co-workers[68] have published an excellent illustration of this lesion. Since the skin in Rapaport, Herman and Lehman's[92] patients did not become entirely normal, it is possible that some nutritional factor other than vitamin A plays an accessory but probably lesser role in its etiology.

Sjögren's Syndrome

Sjögren[96] in 1933 described the eye disorder and the commonly associated mucous membrane changes now known as Sjögren's syndrome. A similar clinical syndrome has also been described by Jonathan Hutchinson.[97] Dryness of the skin and mucous membranes resulting from deficient secretion of the glands, particularly the lacrimal, salivary, upper-respiratory and sweat glands, and the glandular apparatus, characterizes this disorder. Keratoconjunctivitis sicca, xerostomia, rhinopharyngotracheobronchitis sicca with impairment of the act of swallowing and of the olfactory and gustatory senses, deficient sweating, achylia gastrica and various other symptoms result from the deficient secretion of these glands. The syndrome occurs most commonly in women of postmenopausal age. Chronic polyarthritis exists in many cases. Bilateral parotid-gland swelling, sometimes remissive and occasionally persistent, may follow the xerostomia.[98–101] In a general sense, the name "Sjögren's syndrome" appears to be applied to the symptom complex of dryness of the cornea and conjunctivas and of the oral and upper-respiratory mucous membrane, with or without an associated enlargement of the

parotid glands. Keratoconjunctivitis sicca is more commonly present alone than with the entire syndrome. Bruce[98] reported 14 cases seen in New York City; only 4 had the complete syndrome.

Stahel[99] considers Sjögren's syndrome a manifestation of vitamin A deficiency with resultant disturbances in ectodermal and endodermal tissues. He treated a patient with vitamin A over a period of months, with striking improvement. The olfactory and gustatory functions became normal, swallowing became easier, sweating returned, and the conjunctivas returned to normal. In Sutton and Sutton's[102] textbook of dermatology Sjögren's syndrome is classified etiologically as avitaminosis A. Sulzberger[103] noted that a patient with Sjögren's syndrome improved with vitamin A therapy, but not with most other vitamins or with iron therapy. Dryness of the corneas and conjunctivas has long been considered a manifestation of vitamin A deficiency. In this condition it appears to result from diminished lacrimal secretion. That the same deficiency may be a cause of the other features of this syndrome apparently represents a new opinion. The few successful therapeutic reports mentioned are at least suggestive of its validity. A final opinion awaits additional studies. Although Sjögren's syndrome is not predominantly one of the skin, mention of it is made here to stress the widening concept of clinical disorders attributable to avitaminosis A.

Miscellaneous Conditions Attributed to Vitamin A Deficiency

In addition to the previously mentioned disorders, which have already been reported frequently enough to justify their receiving significant attention, there are a number of isolated reports of miscellaneous conditions. These warrant consideration because they all seem to point to a common denominator.

Sulzberger and his associates, Goodman, Kanof and Baer,[94, 104] used large doses of vitamin A varying from 30,000 to 500,000 *U.S.P.* units per day over periods of several months, with improvement in cases of dryness of the skin, mild ichthyosis, keratosis pilaris and brittleness of the nail. They also noted with the same therapy that in some cases of dryness and brittleness of the hair the latter resumed a normal sheen and appearance.

Goodman[104] thinks that vitamin A deficiency can produce a picture which is like pseudopelade. Of 10 patients seen by him, all but 1 had keratosis pilaris associated with the scalp lesion. He did not expect the atrophic area of the scalp to respond to vitamin A therapy, but noted definite improvement in the lesions elsewhere on the body.

Sulzberger and his co-workers[94, 104] noted similar results for lichen spinulosus with folliculitis decalvans, a scalp disorder resembling pseudopelade in its end result, patchy atrophy, but differing from pseudopelade in that it presents in its active stages a pronounced element of follicular inflammation including pustulation. Garfield[105] used vitamin A therapy for 2 patients with lichen spinulosus with good results.

The similarity of the histology of the lesions in keratosis blennorrhagica (the dermal syndrome seen occasionally in patients with gonococcal infection, particularly when systemic and severe) with those of keratosis follicularis of avitaminosis A led Combes and Behrman[106] to study the effect of vitamin A therapy on this skin eruption. There was a striking improvement in the skin lesions of their patient after other forms of therapy had failed. They raised the question whether keratosis blennorrhagica might not occur in patients with gonorrhea who had in addition some disturbance in vitamin A metabolism. This point obviously cannot be settled by a single favorable case report, and confirmation is awaited.

Straumfjord[107] has presented preliminary observations suggesting that vernix caseosa may be a manifestation of vitamin A deficiency in the newborn. He questions whether vernix caseosa is a normal substance because many normal babies are born with none. Its occurrence on the palms and soles seems to rule out its derivation from the sebaceous glands. Twenty-five women received up to 100,000 *U.S.P.* units of vitamin A through six months of pregnancy. Twenty-one had babies with little or no vernix, and only 4 had babies with moderate or much vernix. Thirty-one women received no additional vitamin A other than what their diet contained. Twenty-three of these had babies with moderate or much vernix. This interesting report awaits confirmation by others.

Mandelbaum and Schlessinger[108] proved that vitamin A could be absorbed through the intact human skin in physiologically significant quantities, their evidence being the restitution toward normal of dark-adaptation curves in night-blind subjects experimentally deficient in vitamin A when the ointments containing vitamin A were rubbed into the skin. They suggest this as an alternative route to parenteral injection when intestinal absorption is impaired, and think that the specific cutaneous lesions of vitamin A deficiency may respond favorably to this form of therapy. The favorable report by Baer and Vogel,[95] who used a vitamin A ointment in the treatment of dry skin and ichthyosis, supports this contention.

The rapidly increasing number of conditions — all characterized by abnormalities of keratization of the epithelium of the skin — for which vitamin A therapy has proved helpful or curative suggests that ideas concerning what constitutes vitamin A deficiency are undergoing some remarkable changes. "Dysvitaminoses" as postulated by Sulzberger and Cope[109, 110] to indicate abnormal conditions of demand, utilization and transport of vitamins may prove to be more important and prevalent for vitamin A than the simple dietary deficiency of this vitamin stressed so much in the literature of the last few years.

In summary, it should be recalled that skin lesions attributed to vitamin A deficiency for the most part respond slowly to therapy and require large doses (50,000 to 200,000 or more *U.S.P.* units per day) for months and perhaps years. Large doses of vitamin A may be required continuously to maintain improvement. Oral therapy is not always efficacious, the parenteral route at times being required. The deficiency in many cases seems to depend on abnormal metabolism by the body rather than on a deficient diet. A familial tendency to inherit this abnormality of vitamin A metabolism appears to be not uncommon. Night blindness is rarely a subjective complaint; a dark-adaptation test is usually necessary to elicit its presence, and it may be completely absent although the skin lesions are of marked degree. Xerophthalmia of severe degree appears to be uncommon. The mechanism responsible for the many different patterns that an end organ such as the skin may manifest in response to the same vitamin deficiency is not clear. The entire group of disorders characterized by abnormalities of keratosis appears one for much promising research.

Cheilosis and Angular Stomatitis

Observations by Stannus[111] in 1912, and later by others, suggested a nutritional disturbance as a cause of various changes in the lips that have been called cheilosis or cheilitis. To Sebrell and Butler[112] goes the credit for the demonstration that it may occur in riboflavin deficiency. This they accomplished by demonstrating its development in subjects with experimentally produced riboflavin deficiency and its specific subsidence when riboflavin was added to the diet. Sydenstricker,[113] Spies[114] and Jolliffe,[115] with their co-workers and others, confirmed and extended Sebrell and Butler's observations. I[116] have elsewhere reviewed in detail the clinical picture of riboflavin deficiency.

The recent literature indicates that the relation of cheilosis to ariboflavinosis is not so clear-cut as was originally believed. Smith and Martin[117] noted its disappearance in 3 patients with pyridoxine therapy. Hou[118] suggested that ariboflavinosis together with an associated subclinical deficiency of niacin is required to produce marked degrees of cheilosis. Machella[119–120] has considered this subject in detail. He studied patients with cheilosis who manifested no other features of the ariboflavinosis syndrome and who did not respond to riboflavin. He concluded that cheilosis is not always due to riboflavin deficiency alone. It may occasionally respond to pyridoxine or niacin, or may require the entire vitamin B complex in the form of yeast or liver extract. He noted further that hemorrhagic cheilosis may respond only when ascorbic acid is added to the therapeutic regime. Both pyridoxine and pantothenic acid have been suggested as necessary for the proper metabolism of riboflavin, thus affording a possible explanation of the inconstant response of cheilosis to riboflavin therapy.

There are many other causes of changes in the lips[121–123] besides vitamin deficiency, as a glance through any standard dermatology book or the *Quarterly Cumulative Index Medicus* will reveal. Sulzberger and Goodman[124] emphasize the importance of sensitivity to lipstick as a cause of cheilitis in women. When isolated cheilitis in a woman is seen, this possibility must certainly be considered. Sensitivity to dental plates,[125] chewing gum,[126] toothpaste,[127] mouthwashes,[121] cigarette-holders,[121] throat lozenges,[128] the reed used in the mouthpiece of a musical instrument[129] and other agents have been reported as causing cheilitis. Exposure to sun, even in men, may produce cheilitis.[130] In women, it may exacerbate or initiate sensitivity to lipstick. Cheilitis is considered by some as part of the Plummer–Vinson syndrome.[131]

An early lesion in riboflavin deficiency is maceration at the commissures or angles of the mouth, which may result in superficial transverse fissuring, resembling the perlèche so well known to the dermatologist. This characteristic lesion has been referred to as the angular stomatitis of Stannus and as Sebrell's lesion. It may precede or accompany changes in the lips (cheilosis).

The resemblance of nutritional angular stomatitis to the dermatologic entity perlèche has not gone unnoticed. Sulzberger and Cope[109] believe them to be distinct disease entities. Sutton and Sutton[132] stress the frequency of perlèche in childhood and also the commonness with which various bacteria and fungi can be isolated from this lesion. Spies and his co-workers[114] found nutritional angular stomatitis to be as frequent in children as in adults, and furthermore readily cul-

tured *Staphylococcus aureus* or *Streptococcus haemolyticus* from the fissures in most cases. They found that infection subsided spontaneously without chemotherapy as the fissures healed with nutritional therapy. The likelihood that the infection of perlèche is related to ariboflavinosis in a manner analogous to the fusospirochetosis of pellagrous stomatitis has been discussed by Sutton and Sutton. The striking therapeutic success noted by Spies and his co-workers[114] appears to give some weight to the Suttons' contention.

Unfortunately, not all commissural fissures are nutritional — a situation more evident in private practice than in the clinic. Labial fissures may follow trauma from manipulations about the lips by a dentist. Weisberger[133] has noted angular fissures to be common in persons with ill-fitting dentures, due no doubt to the constant drooling of saliva that resulted. The fissures showed no improvement following treatment with riboflavin or vitamin B complex, but responded readily when the dentures were changed so as to eliminate the drooling. Ellenberg and Pollock[134] have likewise been impressed with the importance of poorly fitting dentures in causing angular fissures. They emphasize the frequent association of glossitis with the labial lesions. They call the syndrome "pseudo-ariboflavinosis." Suitable dental treatment is recommended.

Purpura of Vitamin-Deficiency Origin

Vitamin C, vitamin K and probably vitamin P deficiency produce a hemorrhagic diathesis. The differences and similarities in the dermal manifestations of the purpura in these three deficiencies will be briefly reviewed. Other aspects of their hemorrhagic diathesis will not be considered. It should not be overlooked that many causes for purpura other than these deficiencies exist.

Vitamin K Deficiency

The importance of vitamin K as a precursor for the formation of blood prothrombin and the maintenance of normal hemostasis is now well known, as is the frequency with which purpura due to vitamin K deficiency occurs in obstructive jaundice, biliary fistula, liver disease, sprue, chronic diarrhea and high fever and in the newborn.

Bacterial synthesis of vitamin K in the intestinal tract probably accounts for the rarity of hypoprothrombinemia arising solely from a deficient diet. A few probable cases have, nevertheless, been reported. Kark and Lozner[135] studied, under controlled conditions, 4 patients with a mild degree of hypoprothrombinemia; they had multiple nutritional deficiencies but not liver or intestinal disease. Their prothrombin levels returned to normal on the administration of oral vitamin K without bile salts. Scarborough[136] made a similar study of 18 nutritionally deficient patients. He emphasized that nutritional hypoprothrombinemia could be demonstrated by the dilution method for prothrombin of Kark and Lozner but not by the Quick technic. In none of these cases was the prothrombin low enough to have caused bleeding. Aggeler, Lucia and Fishbon[137] report the case of a thirty-two-year-old woman with severe anorexia nervosa with purpura. Her prothrombin concentration by the Quick method was 15 per cent. No organic liver or intestinal disease was present. The purpura did not respond to ascorbic acid, but did to vitamin K, with a resultant rise in prothrombin concentration. This case appears to be an exception, but the circumstances were extreme.

It must be extremely rare for deficiency of vitamin K in the diet alone to cause purpura. Nevertheless, it may assume importance when additive to other factors interfering with normal vitamin K metabolism.

Skin purpura in vitamin K deficiency may be striking. Ecchymoses and suffusions of blood are common, and may at times cover large areas of the skin.[138] They are especially prominent over pressure areas and lack the orthostatic tendency common in scurvy. Subcutaneous hematomas or ecchymoses about needle punctures in the antecubital fossa or ear lobe are frequent, a diagnostic point emphasized by Kark and Souter.[139] Generalized petechial hemorrhages and perifollicular hemorrhages on the extremities do not occur.[138, 140] "Bleeding may occur from the gums after slight trauma, but the gums themselves do not show the purple sponginess characteristic of scurvy."[138] The bleeding time is usually normal and capillary fragility is unaltered.[138] Diagnosis depends on a diminished prothrombin level in the blood and the characteristic response to vitamin K therapy.

Vitamin P Deficiency

Szent-Gyorgi in 1936 postulated the existence of vitamin P, a flavone substance, so named because it regulated capillary permeability. It has been prepared in relatively pure form as citrin, which consists of at least two substances of the benzapyrone type — hesperidin and demethylated hesperidin (eriodictyol glycoside or eriodicitin), the latter probably being the more active form.[141] There has been considerable controversy concerning the exact chemical nature of vitamin P, the capillary-permeability specificity claimed for it, the ability to produce its deficiency experimentally in animals and the therapeutic results claimed for its clinical use.

Lindheimer, Hinman and Halliday[141] in a recent paper critically reviewed the now rapidly expanding controversial literature on this subject. In the part of their conclusion that is of clinical import they state, "Human clinical studies show that citrin has a definite effect in improving low capillary resistance in various conditions, whether of known dietary origin or not." Zacho,[142] Ruszynák and Benko[143] and Bacharach[144] all report the production of lowered capillary resistance in guinea pigs and rats receiving a scorbutogenic diet containing large daily doses of pure ascorbic acid but lacking in vitamin P. Treatment of these deficient animals with citrin but with no other change in the experimental setup resulted in restitution of capillary fragility to normal over a period of days.[143]

The papers by Kugelmass,[145] Jersild,[146] Scarborough,[147] Rapaport,[148] and others are typical of those reporting worthwhile therapeutic results in clinical practice. Jersild suggested that Schönlein–Henoch's purpura may be due to vitamin P deficiency. Scarborough found vitamin P useful in the treatment of purpura senilis. The valid criticism that treatment of clinical patients is difficult to control and evaluate seems effectively answered by Scarborough, who not only produced isolated P avitaminosis in man but has also attempted to delineate a specific clinical picture for it.

Two experimental subjects suffering from nutritional deficiency were placed for several months on a vitamin-free diet, supplemented by chemical vitamins including large doses of ascorbic acid but no vitamin P. There was a progressive increase in capillary permeability, and petechial hemorrhages appeared on the legs (orthostatic), in pressure areas and after the application of a tourniquet. Various symptoms were noted. The large subcutaneous hemorrhages or bleeding gums seen in scurvy did not appear. Institution of vitamin P therapy relieved the symptoms within forty-eight hours, no further petechial hemorrhages developed, and the capillary resistance progressively returned to normal. The course of the experiment, the findings and the response to therapy were similar in both subjects. This ingenious experiment, although apparently conclusive, awaits confirmation. Scarborough also treated several scorbutic patients under similar controlled conditions, giving vitamin P but withholding vitamin C, with similar improvement in capillary resistance. He concluded that "administration of vitamin P can produce an increased capillary resistance in the scorbutic subject either before or after treatment with ascorbic acid."

Scarborough noted circumpilar (perifollicular) petechial hemorrhages in his pure vitamin P-deficient subject, thus questioning the specificity of this finding for the clinical diagnosis of scurvy. Except for a positive test for lowered capillary resistance and a slightly increased bleeding time (Duke[149]), an exhaustive hematologic investigation of the two experimental subjects was entirely normal.

The clinical picture of avitaminosis P as postulated by Scarborough is one of much decreased capillary resistance, petechial hemorrhages, spontaneous or over pressure areas (being at times circumpilar in location), a slightly prolonged bleeding time (Duke) and varying subjective symptoms, such as pain in the legs on exertion, pain across the shoulders, weakness, lassitude and fatigue, all responding to specific vitamin P therapy. Scarborough adds that since the exact chemical nature of vitamin P used by him is still unknown, its therapeutic use should be limited to experimentally controlled conditions.

Vitamin C Deficiency

That the concept of scurvy has its roots in antiquity is clearly shown in the excellent reviews by Ralli and Sherry[150] and Faulkner.[151] The purpuric manifestations commonly considered diagnostic of scurvy are based on the study of the disease as seen in the clinic or in private practice, the descriptions not varying widely over the years. It is a truism that a pure vitamin deficiency is a rarity in clinical practice, and the scorbutic patient as ordinarily seen is very likely to have some associated nutritional disturbance. It is worthwhile, therefore, to review the type of purpura seen in scurvy when other deficiency factors are known and controlled.

The classic experiment by Crandon, Lund and Dill,[66] in which Crandon lived for six months on an experimentally controlled diet deficient only in vitamin C, with resultant production of pure scurvy, serves as the keystone for analysis of this question. A significant number of moderate-sized perifollicular hemorrhages occurred, which did not fade on pressure and were not elevated, appearing first on the lower leg and then on the thighs (an illustration of them appears in their paper). An orthostatic tendency was demonstrated, since they were numerous when Crandon was on his feet for several hours. The experiment did not continue long enough to produce gross ecchymosis of any degree. The gums were essentially nonhemorrhagic, relatively firm and not "heaped up." The Gothlin, Dalldorf and Rumpel–Leeds tests were negative, indicating normal capillary resistance. The Ivy bleeding time remained normal throughout. Other hematologic data relative to hemostasis were normal. The perifollicu-

lar hemorrhages and other skin manifestations cleared promptly on institution of vitamin C therapy.

The lack of bleeding spongy gums in scorbutic infants before eruption of the teeth and in scorbutic adults who are edentulous is well known. Crandon's experiment indicates that bleeding gums in scorbutic adults may likewise be absent if the teeth and gums are otherwise healthy before the deficiency commences. The heaped-up, spongy, bleeding, purplish gums so common in clinical scurvy probably represent vitamin deficiency in addition to pre-existent gingival and dental disease. Although the gums may bleed in vitamin K deficiency when traumatized and more rarely spontaneously, they are never purplish, spongy or swollen as in scurvy.[138] According to Scarborough,[149] the gums were normal in his patients with avitaminosis P.

This experiment indicates that the capillary-fragility test may be normal during frank scurvy. If the concept of capillary permeability control by vitamin P is true, it would further indicate that Crandon did not have an associated vitamin P deficiency with his scurvy. Rapaport[148] lists six groups of investigators who were unable to correlate increased capillary fragility with states of vitamin C deficiency. Yet a positive tourniquet test with production of showers of petechiae is often seen in frank clinical scurvy.

Except under very special circumstances, Scarborough[147] has not found ascorbic acid capable of increasing capillary resistance. Extravascular suffusion of blood into the tissues, whether occurring in the course of the disease or produced artificially, has been found temporarily to increase capillary resistance in clinical scurvy, which he considers a "complex deficiency state."[152] This observation incidentally affords some rationale for the common empirical practice of injecting intramuscularly some of the patient's own whole blood for various hemorrhagic disorders.

Davidson[153] kept 2 scorbutic patients on a vitamin C-free diet under controlled conditions. Therapy with crude vitamin P (assayed to demonstrate the absence of vitamin C) restored the tourniquet test to normal, but had no effect on the perifollicular hemorrhages and ecchymosis of the legs. The latter cleared only with vitamin C therapy. Scarborough[147] has reported several similar experiments, as have Cameron and Mills.[154] Levcowich and Batchelder[155] report that 2 girls kept on a scurvy-producing diet supplemented with crystalline ascorbic acid manifested petechiae that became less prominent when "natural sources" of vitamin C were substituted for the crystalline ascorbic acid.

The specificity of perifollicular hemorrhages for scurvy seems questioned by Scarborough's observation that circumpilar petechiae (evidently the same thing) appeared in his 2 patients with supposedly pure vitamin P deficiency. As mentioned before, his experiments are still unconfirmed. It appears that ecchymoses and other soft-tissue bleeding are the most characteristic purpuric manifestations of true scurvy.[149]

Table 3 summarizes the pertinent features of the purpuras associated with deficiencies of vitamin K, vitamin C and vitamin P in human beings and is based on data available in the literature. These differential features must for the present be considered as only tentatively correct, since they depend in part on a number of unconfirmed observations.

Palmar Erythema

Perera[156] describes palmar erythema as "a symmetrical, erythematous, capillary and arteriolar dilatation involving the eminences of the palms and the digits of the hands, rarely the soles, at times extending over the fingertips to the nailbeds and lateral distal phalanges." It has the appearance of a diffuse or blotchy redness. In milder stages the palmar eminences alone may be involved. The erythema blanches on pressure and the skin feels warmer to touch than usual. Walsh and Becker[157] and Bean[158, 159] have reviewed this subject in detail. Their papers contain excellent illustrations of palmar erythema.

Because of its frequent presence in persons with portal cirrhosis, palmar erythema has been called "liver palms."[160] It also occurs in pregnancy [156, 157, 159, 161] and in a miscellaneous group of conditions most of which are characterized by malnutrition.[156, 159] Associated signs of deficiency, such as cheilitis, glossitis and peripheral neuritis, have been noted in some patients.[156] The not uncommon association of spider angiomas and palmar erythema in the same person has been emphasized by Walsh and Becker[157] and Bean.[159] The disease may occur in normal persons but is rare.

Perera[156] considers the cause obscure, but stresses its common association with chronic disease and prolonged dietary insufficiency or deficiency states. He reports that intense multiple-vitamin therapy did not generally relieve it, which has been my experience at Boston City Hospital.

Bean[158] believes that palmar erythema may result from abnormal metabolism of the 17-ketosteroid hormones. He produced not only palmar erythema but also spider angiomas following administration of potent estrogens to a patient with cirrhosis. On discontinuance of the estrogens both conditions gradually disappeared. In a more re-

TABLE 3. *Differential Features of Purpura of Vitamin-Deficiency Origin.*

Differential Features	Vitamin K Deficiency*		Vitamin C Deficiency	Vitamin P Deficiency
	Latent hemorrhagic hypoprothrombinemia (bleeding only after trauma)	Spontaneous hemorrhagic hypoprothrombinemia (spontaneous bleeding)		
Chief reason for development of the vitamin deficiency	Liver disease, obstructive jaundice, sprue, diarrhea, high fever, infancy (newborn) and so forth	Liver disease, obstructive jaundice, sprue, diarrhea, high fever, infancy (newborn) and so forth	Dietary deficiency	Dietary deficiency
Factors conditioning the appearance of the purpura	At sites of obvious trauma, such as recent wounds (operative, traumatic and so forth), intestinal ulcers (ulcerative colitis), needle-puncture areas of skin, vigorous brushing of teeth and so forth	Appears spontaneously, with little or no trauma in skin, mucous membranes, brain, uterus and so forth	Orthostatic in legs from pressure or trauma to skin; may also appear spontaneously without obvious trauma.	Orthostatic in legs; may appear spontaneously or follow pressure on the skin.
Dermal manifestations of the purpura	As above: needle-puncture ecchymosis or hematoma is the most characteristic skin lesion in the average patient; no petechiae.	Ecchymoses and suffusions of blood in skin, especially over pressure areas; skin purpura not always a prominent feature; may be minimal although serious internal bleeding is present; no petechiae.	Ecchymoses of skin and soft tissues; perifollicular hemorrhages.	Petechiae the chief lesion; may be spontaneous or appear over pressure areas; may be perifollicular in location.
Spontaneous mucous-membrane bleeding	Absent	Present	Present	Absent
Gums	Normal; no bleeding except from trauma.	Gums relatively normal in appearance; may appear hemorrhagic and bleed spontaneously but are not heaped up, spongy or purplish.	In association with gingival disease are spongy, heaped up and purplish; may be normal in the edentulous or well-kept mouth.	Normal
Perifollicular localization of hemorrhagic diathesis	Absent	Absent	Present	Present
Blood prothrombin level	Below 35 per cent of normal	Below 20 to 15 per cent of normal	Normal	Normal
Clotting time	Generally normal	Commonly prolonged	Normal	Normal
Clot retraction	Normal	Normal	Normal	Normal
Plasma and white-cell-platelet vitamin C content	Normal	Normal	Very low to absent	Normal
Bleeding time (Duke)	Normal at the time of test; bleeding may occur from the puncture wound after an interval of time.	Usually normal, occasionally prolonged; bleeding may occur from the puncture wound after an interval of time.	Normal	Slightly prolonged
Platelet count	Normal	Normal	Normal but may be somewhat diminished at times (values as low as 100,000 per cubic millimeter have been noted clinically†)	Normal
Tourniquet test (Rumpel-Leeds) — petechiae appearing after application of a tourniquet to the arm	Normal	Normal	Normal	Strongly positive; many petechiae appear below level of the tourniquet.
Comment	A slight diminution of the prothrombin content of the blood may result from a pure nutritional deficiency of vitamin K, but probably never or only rarely will it be of a degree sufficient to cause bleeding; it may, however, be additive to the causes listed above.		Scurvy, as seen clinically, may represent varying combinations of the features of both these deficiencies.	

*Based on Kark and Souter's[139] classification of hypoprothrombinemia.

†C. S. Davidson: personal communication.

cent paper Bean[159] gives the results of his clinical study of 11 patients with palmar erythema. He noted that cutaneous vascular "spiders" occurred in 8 of the cases and that they waxed and waned concomitantly with the degree of redness of the palms. He postulated that both these localized vascular disturbances may result from an abnormality in circulating estrogenic substances and other 17-ketosteroids.

Lofgren[161] in a similar type of experiment gave large doses of estrogen to a woman for seven days when she was four months post partum, and reproduced the palmar erythema that had been noted during pregnancy and had faded after delivery. He subscribes to the hormonal origin of palmar erythema.

Other work has been reported that links the action of estrogenic substances with vitamin B metabolism. Ashworth and Sutton[162] reported observations suggesting that estrogens either increase the demand for or suppress the utilization of the vitamin B complex. They found that the administration of estrogens to persons with a subclinical vitamin B complex might cause the appearance of lesions characteristic of thiamin, niacin and riboflavin deficiency. Biskind[163] suggests that syndromes related to an excess of estrogen, such as menorrhagia, metrorrhagia, cystic mastitis and premenstrual tension, are caused by failure of the liver to inactivate estrogen because of deficiency of the vitamin B complex. He reports successful treatment of these endocrine syndromes with vitamin B complex. Hence, the possibility that estrogens produce palmar erythema by interfering with the normal metabolism of some factor of the vitamin B complex cannot be disregarded.

Although its exact cause is not entirely clear, the frequency with which palmar erythema is seen with liver and deficiency disease is worthy of comment.

Dyssebacia

Smith, Smith and Callaway[164] have reported studies on a disorder of the sebaceous glands in pellagrins that they called "dyssebacia." In addition to the typical dermatitis, many pellagrins show skin lesions involving the sebaceous glands. This disease is characterized by the development of plugs of sebum that project from the dilated orifices of the sebaceous follicles, giving the skin a rough (shark-skin) appearance. The skin is dry from failure of the natural oily sebum either to evolve or to reach the surface. It responded readily to autoclaved yeast or crude extracts of liver, but poorly to thiamin and riboflavin and only moderately well to niacin. Smith et al. concluded that dyssebacia results from a deficiency of some factor or combination of factors present in the vitamin G complex.

Jolliffe, Rosenblum and Sawhill[165] observed the presence of dyssebacia in many patients with pellagra and ariboflavinosis and in some alcoholic patients not manifesting evident deficiency disease. A good therapeutic effect resulted from the use of whole B complex in the form of a good diet and brewer's yeast, Vegex or yeast concentrates. In their search for the significant factor controlling dyssebacia, they treated subjects with persistent postadolescent acne with pure pyridoxine. The oral administration of this vitamin resulted in some cases in clearance of the acne. A most striking finding, noted in practically all the cases, was the marked reduction in the oiliness of the skin, even to the point of actual dryness and scaling. These writers suggest that the physiologic function of pyridoxine may be connected with utilization of the unsaturated fatty acids.

It is apparent that there are a number of abnormalities of the sebaceous-gland function that may result from nutritional deficiency. Gyorgy[9] and Gross[8] have emphasized the possible relation of the seborrheic type of skin disorders to deficiencies of the vitamin B complex. The full therapeutic implication of these investigations remains to be determined, but it appears to offer promising possibilities.

Scarborough,[166] in an article appearing since this review was prepared, states that he has seen a number of patients with the clinical syndrome of vitamin P deficiency. All showed petechial hemorrhages, increased bleeding time, a positive tourniquet test and a slightly lowered serum calcium. The condition was cured in each case with vitamin P therapy. He believes that the vitamin P effect on the capillary walls is mediated in some indirect way, possibly connected with liver function. Hesperidin administered by mouth increased the urinary elimination of glycuronates.

Bacharach[167] has been able to assess the vitamin P activity of extracts in terms of provisional units.

80 East Concord Street

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor**
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CASE 29221

PRESENTATION OF CASE

A forty-nine-year-old man, a grocery clerk, entered the hospital because of crampy abdominal pain.

Two months prior to admission the patient had "bronchitis," from which he never fully recovered as a slight cough persisted. Eight days before admission he developed a slight head cold and that evening took two tablespoonfuls of Epsom salts, although his bowels had always been regular. He was awakened at 5:00 a.m. with sharp, crampy, "agonizing" pains in the abdomen that intermittently occurred throughout the day at ill-defined intervals and gradually localized in the right side of the abdomen. After three days he felt better, but three days prior to admission the pain returned and seemed to localize in the right upper quadrant. On the day before admission his physician found a "mass" in the right side. At no time was there any nausea, vomiting, gas, anorexia, chills, fever, change of bowel habits or bloody, tarry or acholic stools. For many years the patient had had nocturia (two to four times) without any other urologic symptoms. During the present illness he had lost 10 to 15 pounds, which he attributed to a "light diet."

The family and past histories were noncontributory.

Physical examination revealed a well-developed and well-nourished man who complained of sharp pains in the right upper quadrant but who did not appear to be uncomfortable. The chest was hyperresonant. The heart and lungs were normal. There was slight tenderness in the right side of the abdomen at the level of the umbilicus, where a grapefruit-sized mass was easily felt, which moved slightly with respiration but did not seem to be attached to the liver. The surface markings and consistence of the mass could not definitely be made out. No other masses were felt. The prostate was slightly enlarged, soft and nontender.

The blood pressure was 145 systolic, 80 diastolic. The temperature was 101°F., the pulse 84, and the respirations 20.

*On leave of absence.

Examination of the blood disclosed a white-cell count of 12,000. The urine was acid in reaction, had a specific gravity of 1.015, and gave a + test for albumin; the sediment contained 15 white cells per high-power field. A stool was guaiac negative. The blood Hinton test was negative. The blood protein was 4.5 gm. per 100 cc., and the chloride 99.7 milliequiv. per liter; the prothrombin time was normal.

A flat plate of the abdomen showed normal kidneys. The psoas contours were not remarkable. No abnormal soft-tissue mass was observed. Intravenous pyelograms showed rapid filling of the pelves and calyxes on both sides, without evidence of distortion. The bladder was normal. A barium enema passed readily from the rectum to the cecum, outlining a normal sigmoid and descending and transverse colon. In the ascending colon on the lateral wall, extending from a point 6 cm. above the tip of the cecum upward for a distance of 8 cm., was a lobulated filling defect that had the appearance of an intrinsic lesion. There was no evidence of obstruction.

On the eighth hospital day an operation was performed.

DIFFERENTIAL DIAGNOSIS

DR. HORACE K. SOWLES: There seem to be a few red herring scattered along this trail. We have a history of "bronchitis" two months prior to entry, which never cleared up, and eight days before entry the patient had a head cold with a temperature of 101°F., not to mention the white-cell count of 12,000 and the 15 white cells in the urine, a picture that perfectly well goes with renal infection, such as pyelonephritis, pyonephrosis or perinephritic abscess. X-ray studies, however, showed that the kidneys were normal and that the psoas muscle was clear. So we can rule out perirenal abscess or mass, and that gives the kidneys on the whole a relatively clean bill of health.

Then we come to the x-ray films of the bowel, which show definite pathology — a fairly large intrinsic tumor of the cecum protruding into the bowel cavity. The tumor was lobulated and, I should say from the description, not ulcerative. If this tumor were ulcerated, that might explain some of the other symptoms, such as the high white-cell count and the fever, but one would also expect guaiac-positive stools, which were not recorded. With an ulcerated tumor of the cecum one usually finds a definite blood picture in the form of anemia, but there was no evidence of that. The x-ray film points to a nonulcerating lesion, which Dr. Holmes will tell us more about.

DR. GEORGE W. HOLMES: In this film the kidneys are fairly well seen. They do not appear to

be large or abnormal in shape. The calyxes are also quite clearly made out, and I should say they are within normal limits. In other words, x-ray examination is negative so far as kidney disease is concerned.

FIGURE 1.

The psoas muscle shows up quite well. The statement about the soft-tissue mass can be interpreted in two ways. I presume that they meant that they did not see a mass on the films, not that it was overlooked. I certainly do not see anything characteristic of a soft-tissue mass in the abdomen, although apparently it was felt.

As one reads the report on the gastrointestinal examination one gets a different idea from that obtained by looking at the films. Certainly this is not the characteristic angle of deformity that is seen in carcinoma of the colon. This film (Fig. 1) appears to bring out the lesion as well as any. There seems to be a mass of considerable size along the outer margin of the bowel, just above the cecum, perhaps extending into the cecum but not producing obstruction of any kind. The man who did the examination had the advantage of being able to palpate the patient, but my impression is that the mass is extrinsic and perhaps adherent to the wall of the bowel rather than within it.

DR. SOWLES: This mass was in the right upper quadrant, moved with respiration and was not attached to the liver; all this fits in with a kidney mass, presumably inflammatory because of the fever, elevated white-cell count and pus cells in the urine. The various x-ray studies rule out the kidney quite well, but this reasoning may fail us. If the mass is extrinsic, it may be an inflammatory mass associated with infection in the renal tract on the right side, but aside from that one must explain the story of pain that the patient had when he took Epsom salts. Perhaps they were just cramps due to Epsom salts. If the patient had a large lobular pedunculated mass in the cecum, under the stress of the salts he may have devel-

oped intussusception, which may cause crampy pains. I cannot combine the two things. Dr. Holmes, did you say that the lesion was nonulcerative?

DR. HOLMES: I cannot tell. The cecum is not emptied, hence it is impossible to see the mucosa.

DR. SOWLES: I cannot see how a nonulcerative tumor in the wall of the cecum could have been responsible for the elevated white-cell count and fever. The patient may have had a little hangover from the bronchitis and head cold of only eight days before. My translation of the reports of the studies on the kidneys rules them out, and from the x-ray diagnosis I should say, that this was a tumor in the wall of the cecum. Dr. Holmes suggested that it may have been extrinsic, a lobulated polypoid growth protruding into the cecum from the lateral wall. I cannot match up the two pictures sufficiently to come to a more definite diagnosis than that.

DR. FLETCHER H. COLBY: Could this have been an appendiceal abscess?

DR. SOWLES: The lesion was several inches above the tip of the cecum. Of course, one should always think of an appendiceal abscess, because one originating from the tip of a retrocecal appendix could be so located that it would press on the outer side of the cecum.

DR. G. G. SMITH: At this distance it almost looks like a soft-tissue mass opposite the second and third lumbar vertebras.

DR. SOWLES: It does not interfere with the course of the ureter. The edge of the psoas muscle is quite clear.

DR. SMITH: Yes, but over that area it is dimmed a little.

DR. SOWLES: It could perfectly well have been an appendiceal abscess lying on the outer side of the cecum.

A PHYSICIAN: Could a large distended gall bladder produce that picture, Dr. Holmes?

DR. HOLMES: No.

DR. SOWLES: A large distended gall bladder is often low down on the right side.

DR. ARTHUR W. ALLEN: But not behind the colon.

DR. SOWLES: No.

DR. ALLEN: This man came in with what we believed to be an inflammatory mass. There was not much doubt in our minds that it was inflammatory, and since it was in the flank, we thought of kidney and also considered other possibilities, particularly acute appendicitis with abscess formation. The X-ray Department made a diagnosis of an intrinsic lesion in the ascending colon. If this was carcinoma of the ascending colon, we decided that it had perforated and that we were dealing with a perforation with abscess formation. We kept the patient on the ward for about a week; and he improved considerably and the mass was reduced somewhat in size.

We operated under the diagnosis of carcinoma of the ascending colon with perforation, and did a preliminary ileotranscolostomy preparatory to a resection of the whole segment. When the abdomen was opened there was evidence of a good deal of inflammatory reaction. There were obvious fibrin deposits on the small intestine here and there, but we have learned that we must not touch the original lesion by palpation if we are going to do a preliminary ileotransverse colostomy, so this was not handled in any way. The terminal ileum, about 25 cm. from the ileocecal valve, was anastomosed to the midtransverse colon. The patient did well, and three weeks later we proceeded to expose the right abdomen through a separate incision, finding that the primary lesion was an appendiceal abscess, the appendix being turned on itself and occupying the retrocecal position seen in the x-ray films. We removed the appendix,—the abscess was almost completely absorbed by that time,—and the man made a perfectly good recovery.

We have been faced with this situation four or five times, and in at least two of the cases we could not tell until we had resected the right colon that the origin was appendiceal. In this man it was easy enough to determine the true diagnosis as soon as the lateral wall of the cecum was freed. The appendix was obviously the source of the mass and one could easily identify it as being in the subacute stage.

DR. SOWLES: Did you take down the ileotransverse colostomy?

DR. ALLEN: No. There was residual infection in the region, and I believe it was best to let him keep the ileotransverse colostomy. I doubt that it will trouble him in the future.

CLINICAL DIAGNOSIS

Carcinoma of cecum.

DR. SOWLES'S DIAGNOSIS

Carcinoma of cecum.

ANATOMICAL DIAGNOSIS

Appendiceal abscess.

PATHOLOGICAL DISCUSSION

DR. BENJAMIN CASTLEMAN: Microscopic examination of the appendix showed that most of the infection had subsided; there was subacute and chronic periappendicitis with a little invasion of the wall in one spot.

CASE 29222

Presentation of Case

A forty-four-year-old plumber entered the hospital because of intermittent periods of constipation associated with "abdominal distress and nausea."

Approximately ten years prior to admission the patient began to have periods of rather severe constipation that usually lasted two or three weeks and were unrelievel by enemas or cathartics. Frequently associated with the constipation were rather marked abdominal distress and nausea, but no vomiting, except immediately after the use of cathartics. There was no diarrhea, melena, hematemesis or jaundice, and the stools were of normal caliber, consistence and color.

The family history was noncontributory. For many years the patient had had frequent colds with a chronic cough during the winter. Approximately twenty years prior to admission he contracted pleurisy during the summer, which lasted several months and was relieved only by immobilizing the chest with adhesive strapping. There was no history of hemoptysis, night sweats, chills or weight loss.

Physical examination disclosed a well-developed and well-nourished man who seemed comfortable. The heart and lungs were normal. No abdominal masses were felt, and no tenderness or spasm was elicited. Rectal examination was negative.

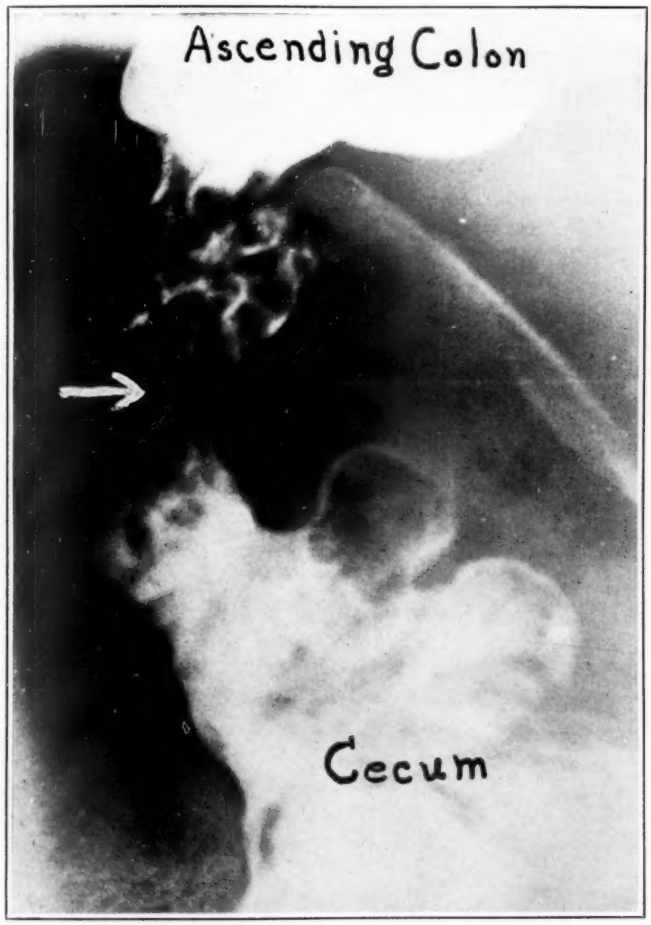

Figure 1. *Spot Film Showing an Area of Narrowing (arrow) in the Right Colon.*

The blood pressure was 90 systolic, 58 diastolic. The temperature, pulse and respirations were normal.

Examination of the blood revealed a hemoglobin of 14.5 gm. and a white-cell count of 8600. The urine was negative. A blood Hinton test was negative. The nonprotein nitrogen was 24 mg. per 100 cc., and the protein 6.1 gm.

A barium enema revealed an area of narrowing approximately 2.5 cm. in length in the ascending colon; it was about 6 cm. distal to the ileocecal

valve and caused considerable obstruction. The mucous membrane was not well visualized but seemed to be ulcerated. The distal margins of the lesion were shelf like, and the area of narrowing was abrupt. The cecum contained considerable fecal material, but the appendix filled rapidly. There was a small diverticulum of the ascending colon proximal to the area of narrowing, and another diverticulum in the distal transverse colon. The terminal ileum filled and appeared normal.

An operation was performed on the fifth hospital day.

Differential Diagnosis

Dr. Edward L. Young: Of course there are only a limited number of probabilities and various possibilities in this case. The probabilities are malignant disease, tuberculosis and diverticulitis, but from the description of the x-ray films it seems to me that the last is ruled out.

How much attention should we pay to tuberculosis? The story of pleurisy is consistent with a tuberculous infection twenty years before entry. We know that tuberculosis of the ileocecal region, where intestinal tuberculosis is most likely to be found, can occur without lung involvement. We also know that the differential diagnosis between it and carcinoma is often impossible. I do not know how much attention to pay to the attacks of severe constipation. Certainly one would not expect such attacks to have been due to malignant disease for a period of ten years. I also question whether it could have been due to tuberculosis.

When they say that the chest was normal do they mean by x-ray or merely by physical examination?

Dr. Benjamin Castleman: By physical examination only. No x-ray film of the chest was taken before operation.

Dr. Young: They apparently did not take the history of pleurisy too seriously.

Then I had better make this short and say that malignant disease is the best bet. Carcinoma? Yes. But one should also remember that a lymphosarcoma is not unheard of in this area. I should pay a good deal of attention to what the roentgenologist said in describing this lesion. If the recorded description is correct, I think that tuberculosis can be discarded, and certainly diverticulitis.

I should like to get more help from the roentgenologist.

Dr. Laurence L. Robbins: The area of narrowing is in the ascending colon. The only thing to suggest diverticulitis is the fact that there is a diverticulum in the ascending colon, but it is not close to the involved area. The spot film (Fig. 1) shows the upper margin of the lesion, which appears to be slightly lobulated; the area of narrowing is only about 2.5 cm. in length. The distal margin appears shelf like, but the proximal margin is funnel shaped. The area of narrowing did not appear to enlarge during examination.

I believe that the lesion was due to carcinoma or tuberculosis.

Dr. Young: I shall simply stick to the theory of probabilities and say that my first choice is malignant disease, with tuberculosis second. I do not believe that it makes a bit of difference so far as the patient is concerned. The only way to treat either, of course, is by resection of the right colon.

Clinical Diagnosis

Carcinoma of cecum.

Dr. Young's Diagnosis

Carcinoma of ascending colon?
Tuberculosis of ascending colon?

Anatomical Diagnosis

Tuberculosis of cecum, with involvement of regional lymph nodes.

Pathological Discussion

Dr. Castleman: This patient was operated on by Dr. Robert R. Linton with a preoperative diagnosis of carcinoma of the cecum. A right colectomy and resection of a portion of the terminal ileum were performed. When opened the specimen showed an annular ulcerating lesion about 7 or 8 cm. from the ileocecal valve that measured 3 to 4 cm. in length. Microscopic examination showed it to be tuberculosis. The regional nodes also showed tuberculosis.

A point that Adams and Parsons* emphasized several years ago when they reviewed the cases of tuberculosis of the cecum at this hospital should be remembered, namely, that in cases of tuberculosis the red-cell count and hemoglobin are almost always normal or near normal, whereas in cases of cancer they are low. In this case the hemoglobin was normal.

*Adams, R., and Parsons, L. J. Tuberculosis of cecum. *New Eng. J. Med.* 224:315-319, 1941.

The New England
Journal of Medicine

Formerly
The Boston Medical and Surgical Journal

Established in 1828

Owned by the Massachusetts Medical Society and Published under the Jurisdiction of the Committee on Publications

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Material for early publication should be received not later than noon on Friday.

The Journal does not hold itself responsible for statements made by any contributor.

Communications should be addressed to the *New England Journal of Medicine*, 8 Fenway, Boston, Massachusetts.

THE VIRUS OF THE SO-CALLED "VIRUS PNEUMONIAS"

The primary atypical pneumonias of nonbacterial origin continue to arouse the interest of clinical and laboratory workers. A review[1] of this subject appeared in the *Journal* last year. Recent contributions bearing on the etiology of this disease are worthy of comment.

At the Rockefeller Institute, in Princeton, New Jersey, Baker[2] recovered from cats with pneumonia a virus that forms elementary bodies. In the form of a suspension of an infected cat's lung, it readily produced typical clinical symptoms and pulmonary consolidation in mice. Baker suggests that this virus may be related to the one causing some of the atypical pneumonias in man. His evidence, however, is rather tenuous. It depends in part on unpublished reports by others of cases of pneumonia occurring in places where there were sick cats, and in part on a small number of complement-fixation tests performed on serums from acute and convalescent patients. The results of the latter are far from convincing.

Further observations tending to implicate sick cats in the transmission of certain cases of atypical pneumonia have been presented by Blake, Howard and Tatlock.[3] They observed within a brief period the occurrence of an acute respiratory disease resembling primary atypical pneumonia in four members of a family and in eleven cats on a farm in Jewett City, Connecticut. From the lungs of one of the cats they recovered a virus capable of producing a similar pneumonia in other cats. Kittens appeared to be more susceptible to this virus than full-grown cats. Unlike the virus described by Baker, this one failed to infect mice, and in this way also differs from most other viruses known to cause infections of the respiratory tract. Suggestive, but not conclusive, evidence was presented to indicate that the respiratory infection in the members of the family was caused by the virus that produced the infection in the cats.

Still another infectious agent has been obtained from cases of atypical pneumonia by Eaton and his co-workers[4] on the West Coast. Their agent was obtained from sputum and from the lungs of patients at autopsy. It produced nonbacterial pulmonary consolidation in cotton rats after intranasal inoculation under light anesthesia. Sputum obtained early in the disease gave lesions in these animals more regularly than did specimens obtained later. Similar material gave negative results after inoculations in many other species of animals, including mice, ferrets and hamsters. Neutralization tests were carried out successfully with the cotton-rat material and the serums obtained from hyperimmunized cotton rats, but only partial or irregular neutralization was observed with con-

valescent serums from cases of atypical pneumonia and with serums from rabbits immunized with suspensions of human lung that had proved infectious for the cotton rat. This infectious agent, which is presumed to be a filterable virus, differs from the psittacosis-like virus that had previously been described by workers in the same laboratory. The authors consider their evidence for the causal relation of the present agent to the commoner form of atypical pneumonia to be incomplete.

Each of the agents described above is recognized by the lesions it produces in animals. Horsfall and his co-workers[5] in the United States Naval Research Unit at the Hospital of the Rockefeller Institute for Medical Research have just described a virus recovered from patients with primary atypical pneumonia that fails to produce recognizable and reproducible infectious lesions in animals. Their agent is recognized by the fact that it stimulates antibodies in animals that are capable of neutralizing a heterologous virus, the so-called "pneumonia virus of mice." It failed to produce lesions in the lungs of mice and rats, in chick embryos and in egg membranes; nor were elementary bodies, inclusion bodies, rickettsias or bacteria recognized in tissues infected with this agent. Their virus was, however, identified as probably the same as, or closely related to, the one isolated by Weir and Horsfall[6] in 1939 from materials obtained from similar cases after inoculation into mongooses. Evidence was also produced to show that the pulmonary consolidation in cotton rats, which they succeeded in producing by the inoculation of sputum from one of their cases, and the development of antibodies against the mouse-pneumonia virus were results of infection by one and the same agent. Serums from acute and convalescent cases of atypical pneumonia, however, failed to show an increase in neutralizing antibodies against the mouse pneumonia virus during convalescence. This failure was explained by assuming that the human antibody response was too small to be measured by the technic employed. The evidence that the Rockefeller workers have actually obtained a virus that is etiologically related to some cases of atypical pneumonia is, at best, only remotely suggestive. Possibly they may be able to discover a more direct and a more convincing way of demonstrating its presence in cases of atypical pneumonia and its relation to the human disease.

The most exhaustive study of primary atypical pneumonia to be reported thus far has just been published by Dingle and the other members[7] of the Commission for the Investigation of Atypical Pneumonia and Other Respiratory Diseases at Camp Claiborne, Louisiana. These workers have presented in great detail the clinical, bacteriologic and epidemiologic aspects of their cases, which on the whole were primarily of the mild variety, similar to those described in a number of previous outbreaks in schools and colleges and among hospital and military personnel. In their attempts to determine the etiologic agents in their cases, these men were aided by many of the most distinguished and experienced investigators in this field, working in different laboratories throughout the country. The results of their searches for causative agents were chiefly negative. They did, however, obtain some evidence to suggest that an unidentified agent was present in some of the cases. Repeated passages of filtered amniotic fluid from chick embryos inoculated with throat washings from certain cases resulted in the development of cloudy amniotic fluids and retardation of the growth of the embryos, with death of a considerable number. No pulmonary lesions were produced on passage of this material through mice. Specimens of sputum and throat washings from four of their patients also produced hemorrhagic lesions in the lungs of cotton rats after intranasal inoculation. No bacteria were cultured from the lesions, and the agent could be passed from one animal to the other by direct inoculation of the lung material but not with the same material after Berkefeld filtration. In occasional lesions, cytoplasmic inclusion bodies were seen. On the basis of their results, Dingle and his co-workers think it

likely that a new agent, probably a virus, was responsible for their cases of primary atypical pneumonia. The studies of this commission are now being continued at Fort Bragg, and should yield even more valuable information in the near future.

From these recent studies it seems fair to conclude that cases of so-called "primary atypical pneumonia" are probably of varied etiology. It seems possible, however, that a single agent may be the cause of many or even most of the cases in a given outbreak, or in a single locality. In any event, the isolation of the causative agent is at best a tedious and painstaking procedure that must be carried out under the most exacting and controlled conditions.

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SELECTION OF OFFICER CANDIDATES

An interesting and provocative study describing a method designed to select those men who possess the fundamental qualities that warrant their training as officers in the armed forces has been recently published by the Department of Hygiene of Harvard University.* The method combines three elements: an eight-minute test of physical fitness, a ten-minute interview to evaluate the man's total personality and, finally, a brief inspection of the body build to determine the characteristics of masculinity that "have been found to be related to physical fitness and officer fitness."

*Woods, W. L., Brouha, L., and Seltzer, C. C. *Selection of Officer Candidates.* 46 pp. Cambridge: Harvard University Press, 1943.

The authors have found that there is a high degree of accord between the results of their comparatively short examinations and the ratings given independently to the same candidates by commissioned officers of the Army or Navy based on a time-consuming study of all available data. There was, further, a remarkably close relation between the level of physical fitness and the evaluation made by the short personality interview. This, in turn, bore a close correlation to the body build. The implication seems to be that the expressions "athlete" and "officer" are to some degree synonymous, but the authors are careful to point out that "the physical fitness test should not be used alone for selection of officers with disregard of characteristics of personality that fit them for combat leadership." In this connection, it should be stated that the study is concerned chiefly with "officer material primarily for field and combat duties," although this distinction is not specifically indicated in the title of the monograph.

In general, the authors conclude that the best officer material is found among men with great physical stamina, as determined by the "step test," those having certain characteristics — such as alertness, steadiness, strength of character and sense of responsibility — that fit them for combat duty, and men with a high "masculine component," as determined by objective examination.

Any of the three parts of the examination is likely to be criticized by those especially interested in that particular aspect of the problem, and no doubt with further experience the criteria may be altered to a greater or less degree. In the meantime, much credit is due the authors for having come forth with a definite and, to some extent, definitive method for choosing those men of the armed forces who are most likely to be competent and responsible combat officers, surely a timely and valuable contribution.

MEDICAL EPONYM

Waldeyer's Ring

This was described by Professor H. Wilhelm G. Waldeyer (1836–1921), of Berlin, at the meeting of the Berlin Society for Internal Medicine on May 5, 1884, in a paper entitled "Ueber den lymphatischen Apparat des Pharynx [The Lymphatic Apparatus of the Pharynx]." This was reported in abstract in the *Deutsche medicinische Wochenschrift* (10: 313, 1884). A portion of the translation follows:

> Since the discovery of the pharyngeal tonsil by Lacauchie, the tubal tonsil by J. von Gerlach, and the establishment of the fact that the follicles of the tongue together represent a superficially spread-out tonsillar structure (the lingual tonsil), it is now evident that a ring of lymphatic tissue surrounds the whole region of the throat and upper pharynx, the course of which may be traced as follows: beginning with the pharyngeal tonsil, it extends to the region around the orifice of the eustachian tube (the tubal tonsil), thence to the faucial tonsil and down along the margin of the glossopalatine arch to the lingual tonsil, whence it crosses to the opposite side and follows a similar path back to the pharyngeal tonsil.
>
> The tonsils simply represent marked accumulations of lymphatic tissue, which is nowhere absent in the above-mentioned region, being demonstrable even in all the intertonsillar spaces. The investigations of the speaker show that the lymphatic tissue also extends deeply into the nares as the center of the middle and lower turbinates and downward onto the posterior wall of the pharynx. This ring of adenoid tissue may be termed "tonsillar ring" or the "lymphatic ring of the throat."

R. W. B.

MASSACHUSETTS MEDICAL SOCIETY

COMMITTEE ON MATERNAL WELFARE

Obstetric Case History: Pregnancy complicated by fibroid — operation

A thirty-three-year-old primipara was first seen when approximately two months pregnant. Her past history was essentially unimportant. She had had no contagious diseases or operations. Physical examination showed a normal and well-developed woman, weighing 120 pounds. The blood pressure was 122 systolic, 60 diastolic. External pelvimetry gave the following measurements: 28, 23 and 21 cm. On vaginal examination the cervix was posterior, and the fundus anterior; the latter was enlarged, and consistent with a pregnancy of eight weeks. Nothing abnormal was found about the uterus by palpation. A blood Wassermann reaction was negative, and urinalyses were normal.

Pregnancy was normal and uneventful until the eighteenth week, when discomfort and pain on the left side of the abdomen were sufficient to awaken the patient from a sound sleep. There was no nausea. The bowels had been regular. When seen, palpation revealed a tumor mass in the left flank, and the uterus seemed irritable. There was no fever. The patient was immediately transported to the hospital and given 10 mg. of Proluton. Her temperature during the first night in the hospital reached 100°F. It was 99.2°F. the next morning, and 99.8 at noon. The white-cell count was 23,000. The mass on the left was tender and seemed quite discrete.

The diagnosis lay between a strangulated fibroid and an ovarian cyst with a twisted pedicle. Consultation was held and operation advised. A flat plate of the abdomen was taken, but was inconclusive. At operation a tumor the size and shape of a medium-sized potato was found arising from the fundus on the left. It apparently was a fibroid and arose from a rather broad pedicle. This was excised, and the base tied with No. 1 chromic catgut. A smaller fibroid, about the size of a plum, on a pedicle was found anteriorly on the left. This was removed in a similar manner. A much smaller one, low down on the right, was also excised. There was practically no bleeding.

The pathological report was as follows: leiomyoma; active acute necrosis with polymorphonuclear infiltration.

Postoperative convalescence was complicated by a temperature of 99.4°F. and a pulse of about 100 for three days. There was little distention, and practically no nausea or vomiting. Subsequently, the temperature remained normal. The stitches were taken out on the tenth day, when the wound was well healed. The patient was discharged on the eighteenth day. Five milligrams of Proluton was given daily during the hospital stay.

The course of pregnancy was normal. Labor started at term. Cesarean was performed because of premature separation of the placenta. The baby weighed 7 pounds, 11 ounces. Convalescence was complicated by a febrile reaction that began on the third day, lasted forty-eight hours and reached a peak of 102°F., with a pulse of 90; this was due to a saprophytic infection. The patient was discharged on the eighteenth day.

Comment. Fibroids occurring during pregnancy are not uncommon and usually are not serious complications. If a fibroid is in the lower segment and is so big that it occludes the pelvic inlet, pelvic delivery is impossible and cesarean section is indicated. Strangulated fibroids, such as the one in this case, are practically always subperi-

toneal and arise from a moderately broad base. Fibroids in the muscle of the uterus rarely become strangulated during pregnancy. Many of them become tender and are painful, but the majority quiet down and do not require surgery.

Operation in this case was advised for two reasons. In the first place, the diagnosis was uncertain. One consultant thought that the tumor was an ovarian cyst and another that it was a fibroid. In either case, the elevated temperature and white-cell count and the tenderness of the tumor indicated surgery. The separation of the placenta, which necessitated cesarean section, occurred during labor when the cervix was not ready for vaginal delivery. When the uterus was opened, more placenta was found to be separated than was thought probable. The uterus was filled with meconium. The membranes were necrotic, and the musculature at the placental site was bluish and rather spongy. There is no reason to infer that the separation of the placenta in any way resulted from the myomectomy.

WAR ACTIVITIES

CIVILIAN DEFENSE

Emergency Medical Service in Industrial Plants

The following directive was recently released by the Medical Division of the Office of Civilian Defense, Washington, D. C.:

Every plant medical department should prepare a "disaster-operations plan" to provide adequate medical service in case of a plant catastrophe involving large numbers of casualties. This is the advice presented in a new bulletin, *Emergency Medical Service for Industrial Plants,* issued by the Medical Division of the Office of Civilian Defense.

The War and Navy departments have urged that plants for which they are responsible plan to use the facilities and services of the Emergency Medical Service organized by civilian-defense authorities. The Medical Division has in turn urged that local chiefs of Emergency Medical Service assist plant medical departments by placing the community medical facilities at their disposal in the event of a major emergency, regardless of its cause.

Pointing out that plant medical departments are not ordinarily staffed or equipped to provide medical service for the large number of casualties that may occur in a major disaster, the bulletin outlines arrangements that should be made to assure adequate medical care at such times.

The disaster-operations plan should provide for necessary first-aid care at the site of the incident, for adequate ambulance service and for hospitalization of the seriously injured, the bulletin advises.

Provision must first be made for casualty stations. Several sites should be selected, in order that alternative locations may be used in case those of first choice are destroyed or rendered unserviceable. An additional site outside the plant should be selected for use in the event of extensive damage to the plant, such as might occur in a bombing or explosion.

The importance of identification and records is especially emphasized in the bulletin.

"In any disaster, confusion will be inevitable," it is pointed out. "It will be difficult, without adequate records, to identify the seriously injured and the dead and to determine the number and names of the missing. The uninjured as well as the injured should be accounted for. A record should be made of every person who leaves the plant. The record should indicate the places to which the injured have been taken."

In a consideration of transportation, the bulletin recommends that arrangements be made with the local chief of Emergency Medical Service to ensure that ambulances under his direction will be made available to the plant should a disaster involve the entire community. Similarly, any ambulance facilities owned by the plant should be made available to the local chief if they are not required at the plant.

Present plans for the hospitalization of industrial accident victims are likely to be grossly inadequate in the event of a major plant catastrophe, the bulletin declares. Large numbers of patients should not be sent to one hospital if other hospitals are available. To provide quick and efficient service to injured persons, casualties should be distributed among various hospitals. Arrangements must be made with the local chief of Emergency Medical Service for the admission of casualties to community hospitals, all of which will be under his supervision during a major emergency.

A prerequisite to the entire plan of mutual aid between a plant and a community is a definite understanding that members of the Emergency Medical Service will be admitted promptly to a plant in an emergency. To assist plant managers to carry out their duty in keeping unauthorized persons out of war-production plants and to facilitate the admission of physicians when they are needed, the service commands of the Army are conducting investigations of the key personnel of the Emergency Medical Service. Personnel investigated and approved by a service command will receive identification cards from the Office of Civilian Defense.

The bulletin sketches the organization and operation of protective services in a community, and the over-all protective services recommended for industrial plants. It also outlines the program of federal compensation for injuries to civilian defense workers and explains how this plan applies to industrial workers. A bibliography of pertinent material is included.

REPORT OF MEETING

NEW ENGLAND PATHOLOGICAL SOCIETY

The second meeting of the New England Pathological Society was held on January 21, 1943, at the Peter Bent Brigham Hospital.

The first paper of the evening, "Simple Tissue Extracts," was given by Dr. Sidney Farber. Acetylcholine may be extracted from normal tissues by treating minced tissue initially with ethyl alcohol, sulfuric acid or trichloracetic acid, and subsequently filtering, shaking with ether and concentrating at low pressure. Although extracts prepared in this manner contain large quantities of other pharmacologically active substances, the presence and amount of acetylcholine may be determined by suitable biologic tests, which permit the exclusion of sub-

stances such as potassium, histamine and adenosine compounds. Since acetylcholine cannot be diffusible freely in tissues in amounts obtained from extracts because of the rapid destruction by choline esterase, it has been suggested that the substance is stored in some special structure that prevents it from diffusing freely through the tissue. Some observations bearing on this point were made in the course of experiments conducted in collaboration with Dr. Ernest K. Landsteiner and Dr. Alfred Pope. It was found that, when small pieces of certain normal organs of the freshly killed rat, guinea pig, rabbit or cat were immersed for a few minutes to a few hours in a bath of Ringer's solution containing physostigmine, there could be demonstrated in the Ringer's solution a substance that had the pharmacologic properties of acetylcholine. All extracts were tested on two preparations of the dorsal muscle of the leech, one of which was eserinized. Verification of the nature of the substance was given by its depressor action, after intravenous injection, on the blood pressure of the cat and the rabbit, with intensification of the effect after physostigmine and disappearance after atropine. The most active extracts were obtained from the intestinal tract. Positive results also were obtained from the brain, the lung, the heart, the bladder and sometimes the kidney. Skeletal muscle, testes, spleen and liver gave negative results. The effects of the pH of the Ringer's solution, the time and the temperature and species differences were studied.

The ready liberation into saline solutions of a substance presumably acetylcholine from decomposing tissue under the conditions employed made it of interest to ascertain whether acetylcholine might be liberated from areas of tissue destruction in the living body. Accordingly, in a series of experiments conducted with the assistance of John Carabitses, intestinal obstruction was produced in rabbits under Nembutal anesthesia by ligation of a large part of the bowel. In the clear fluid that collected in the peritoneal cavity within four to eight hours after the onset of the obstruction a substance was demonstrated that appeared to have the properties of acetylcholine. Greater amounts were observed in the fluid that had collected within the obstructed portion of the bowel and in saline extracts of the necrotic bowel itself. No conclusions were drawn concerning the significance of this finding. Acetylcholine should be added to the group of substances that may be found in extracts of the intestinal tract. This includes potassium, adenosine compounds, histamine and Gaddum's substance P.

The second paper was given by Dr. Charles E. Dunlap, the subject being "Transplantable Osteogenic Sarcomas Induced in Rats by Feeding Radium." Osteogenic sarcomas appeared in the vertebras and pelvic bones in 9 of 13 male Wistar rats after feeding each animal 100 microgm. of radium. Within ten days after feeding, the animals had excreted 95 per cent of the radium. The average amount retained at the end of one year was only 2 microgm. The induction time from the first radium feeding to the discovery of the tumors was 253 to 426 days, averaging 365 days. Two of the nine primary tumors metastasized, one to the pelvic lymph nodes and one to the spleen. Three of the tumors were successfully transplanted to other rats, and one has been maintained through seven serial generations. In addition to the osteogenic sarcomas, all the rats showed widespread necrosis of bone, and atypical new-bone formation was found in all but one. The bone marrow was hypoplastic and showed generalized immaturity and abnormal deposits of hemosiderin. Marked hemosiderosis was present in the spleens, together with extramedullary hematopoiesis. Thus, the pathologic changes consequent to radium poisoning in human beings were reproduced in rats with a fair degree of fidelity and a readily transplantable osteogenic sarcoma of rats was obtained.

In the discussion of the paper the question was raised by Dr. Earle Clark whether the tumor arose from the periosteum or the periphery of the bone. Dr. Dunlap replied that there was a definite question in his mind whether some of them did not arise from the subperiosteal tissue. The question whether similar changes were produced by injection of radioactive phosphorus having a half-life of fourteen and a half days was raised. Dr. Shields Warren stated that although selective deposition in bone of the phosphorus was somewhat comparable, there was not the same effect on the bone structure or the bone marrow. He also pointed out that the radioactivity of phosphorus was due to the beta radiation and that in Dr. Dunlap's cases it was the alpha ray which was responsible for the marrow changes and tumor formation.

The third paper of the evening, "The Effect of Crystallized Bovine Albumin on the Tissues of Normal Animals," was given by Drs. Orville Bailey and Clinton van Hawn. The methods for the fractionation of plasma protein recently developed in the Department of Physical Chemistry of the Harvard Medical School have made available the proteins of blood plasma in states of great purity and in far larger amounts than could have been obtained by previous methods. The albumin of human plasma has already been used in the clinic. To provide larger amounts of material for use in shock, Cohn and Hughes have prepared crystallized albumin from bovine plasma. Before using this material as a therapeutic agent in man, it seemed advisable to determine its effects on animals. Normal rabbits were injected intravenously with crystallized bovine albumin in 25 per cent solution in doses of 1 gm. per kilogram of body weight. Animals were sacrificed at various intervals after one, two, seven and twelve injections. No change in state of nutrition or behavior was noted in the rabbits. Slight enlargement of the spleen was the only change noted grossly. Histologically there was an increase in the amount of phagocytosis of leukocytes and red blood cells in the pulp and sinusoids of the spleen. This was regarded as an accentuation of a process occurring in the spleen normal rabbits. Similar sequences of phagocytosis of blood cells were found in the Kupffer cells of the liver, in lymph nodes and in the bone marrow; in these organs, however, the process took place only to a slight extent. In the kidneys there were swelling and dispersion of the epithelium in the ascending limb of Henle's loop and in the distal convoluted tubules. These changes were regarded as an indication that some of the albumin was filtered through the glomerulus and entered the tubular epithelial cells more rapidly than it was reabsorbed in the circulating blood. The histologic changes in all organs were reversible, the organs eventually returning to a normal state, even after twelve injections.

Mice were injected intraperitoneally with a 25 per cent solution of crystallized bovine serum albumin. A single injection of 1 cc. produced no tissue changes. Thirty similar injections led to slight and rapidly reversible changes in the spleen and kidneys. When 2-cc. doses were injected daily, marked but reversible alterations in the kidneys appeared after ten or more injections. These amounts of albumin were far in excess per kilogram of body weight of the quantities used clinically; however, the studies indicated that the first organ to show evidence of severe injury as the dosage of crystallized bovine serum albumin was increased to excessively high levels was the kidney. No "storage disease" or amyloid

deposition was found in either rabbits or mice under the experimental conditions used.

Because of species differences, it is hazardous to assume that the tissue reactions to crystallized bovine albumin in man are the same as those of the rabbit or the mouse. However, the tissue reactions induced in either experimental animal by injections comparable per kilogram of body weight to those contemplated in man would not contraindicate the use of the material were they to occur in human patients.

In the discussion that followed, the question was raised whether injections of the glomeruli with ice-cold solutions would give more albuminuria, as has been reported by Dock. It was stated that this phenomenon was not observed because only intact animals were used in the experiments.

The fourth paper of the evening, "The Mechanism of Enhanced Diabetes with Inflammation," was given by Dr. Valy Menkin. The enhanced course of the diabetic condition with superimposed inflammation or infection is clinically well known. An inquiry into the basic mechanism concerned in explaining this intensified condition was undertaken by Dr. Menkin. The observations and conclusions drawn are summarized as follows.

The data have been obtained from depancreatized dogs. This form of experimental diabetes has many obvious points of similarity to the human disease. Nevertheless, it is to be recalled that there are also several notable differences. Depancreatized dogs with superimposed inflammation in the pleural cavity induced by previous injection of turpentine tend (with few exceptions) to develop a marked rise in their already existing hyperglycemia. Pleural inflammation per se in nondiabetic animals fails to alter appreciably, or at least in a sustained way, the blood sugar. In depancreatized dogs the presence of a concomitant inflammation has been followed by an average increase of 216 mg. in the concentration of blood sugar. In order to determine the responsible mechanism involved, two considerations have to be kept in mind. In the first place, glucose can be derived to a certain extent from proteins as a result of deamination. Thus, gluconeogenesis from proteins is a well-known phenomenon. It is also important to recall that insulin tends first to repress glucose formation from such noncarbohydrate precursors of glucose. In the second place, proteolysis is a cardinal biochemical feature of inflammation. It is conceivable that the mechanism of enhanced diabetes with superimposed inflammation may be referable to an augmented degree of proteolysis at the site of inflammation with a corresponding increase in glucose formation from products of protein breakdown. The abundant glucose formed at the site of injury in turn diffuses into the circulating blood, thus giving rise to the excessive hyperglycemia. At the same time the enhanced local proteolysis reasonably explains the tendency for the appearance of marked cell damage or increased severity of the inflammatory reaction.

This hypothesis has been fully supported by experimental observations. In brief, the exudate sugar, lactic acid, urea, nonprotein nitrogen, and amino-acid nitrogen have all been found to be markedly increased in diabetic dogs as compared with the levels in nondiabetic preparations. The exudate sugar has increased in the diabetic animals on an average of 47 per cent; the lactic acid, 52 per cent; the urea, 126 per cent; the nonprotein nitrogen, 89 per cent; and the amino-acid nitrogen 74 per cent. At the same time the total protein of exudate in diabetic dogs is on the average 13 per cent lower than that encountered in nondiabetic animals. These facts therefore substantiate the marked increase in proteolysis in the exudates of diabetic animals and the corresponding high glucose content at the sites of inflammation. It is of great significance to note that insulin administration not only lowers markedly the glucose concentration of exudate but likewise represses the increased local proteolysis. This fact strongly supports the view that the excess glucose formation at the site of inflammation seems to be derived primarily from products of protein breakdown. These products as well as the formed glucose are highly diffusible and are consequently not fixed at the site of inflammation. They penetrate readily into the circulation. The result is not merely an exaggerated hyperglycemia; there is also a reflection of the elevated products of nitrogenous metabolism from the exudate into the blood stream. Furthermore, an examination of the leukocytes at the site of inflammation indicates that, with the greater degree of proteolysis and the elevated lactic acid production found in diabetic exudates, these cells show striking signs of injury and degeneration. In this way the combination of lowered pH and enhanced local proteolysis offers an explanation for the increased cell damage of inflammation in diabetic animals.

More recent studies have indicated that abundant glucose at the site of inflammation originates from the injured cells and that the sugar then gradually diffuses into the circulation rather than the reverse order of sequence. Careful comparisons of the sugar concentrations in the exudate and in the blood at various stages of the inflammatory reaction indicate that at first the exudate sugar is at a considerably higher level than the blood sugar. The latter at first shows no appreciable increase over the level found following pancreatectomy. It is only after the reaction in the pleural cavity has progressed for about one day or slightly less that sufficient glucose has diffused from the site of inflammation into the blood stream to reveal a manifest rise in the hyperglycemia. Thus the establishment of a conspicuous gradient in the glucose concentration between exudate and blood supports the view of a gluconeogenetic process at the site of inflammation in the diabetic animal. A similar gradient, although not so pronounced, is found in the case of urea. The evident quantitative difference between the behavior of these two substances seems referable to the difference in the diffusion coefficient of glucose and urea. Observations in nondiabetic animals indicate a transitory gradient in the glucose concentration found in exudate and blood. The provisional nature of the gradient is referable to the marked glycolytic reaction at the site of inflammation, which in the nondiabetic animal quickly overshadows the process of local gluconeogenesis. In this way the essential difference between the diabetic and the nondiabetic animal becomes virtually a quantitative one. The overproduction of glucose at the site of inflammation in depancreatized animals fails to be appreciably affected by glycolysis. The latter reaction, however, in the exudate of nondiabetic dogs soon transcends gluconeogenesis. Nevertheless, these observations point to a basic principle, namely, that inflammation-injured cells per se become potential foci of glucose formation. So far as this particular function is concerned, an area of inflammation therefore assumes to some extent the capacity of the normal liver. This becomes merely exaggerated in an inflamed area of a diabetic animal.

In conclusion, the basic mechanism of diabetes enhanced by superimposed inflammation seems primarily referable to an increased proteolysis at the site of injury. This is followed by excessive glucose formation from nitrogenous sources; the glucose, in turn, diffuses gradually into the circulation, giving rise to a marked hyperglycemia.

In the discussion of the paper Dr. Sidney Farber raised the point whether loss of nitrogen and fat in the stools would produce fatty changes of the lipocaic-deficient type. Dr. Menkin stated that no changes were evidenced when raw pancreas and choline were added to the diet.

BOOK REVIEWS

Aftereffects of Brain Injuries in War: Their evaluation and treatment, and the application of psychologic methods in the clinic. By Kurt Goldstein, M.D. With a foreword by D. Denny-Brown, M.D. 8°, cloth, 244 pp., with 46 illustrations and 2 plates. New York: Grune and Stratton, 1942. $4.00.

The author for many years worked in a special hospital in Germany with patients who had suffered structural injury to their brain during World War I. There he carried on extensive psychologic studies, which were reported from time to time in the German literature. Since coming to this country these studies have been translated into English and now are put together in an attractive volume of outstanding worth. The author's knowledge of the psychology of patients with brain injury is extensive and he gives in detail the findings incidental to his long experience. The book is not for the practitioner but for the specialist in injuries to the nervous system. It will show him the work that has been done in this complicated field and will point out how little we really know about psychotherapy based on structural damage.

The latter part of the book takes up the treatment of patients with severe brain damage, particularly the training of those with speech defects, one of the most marked disabilities that can follow injury. The author is careful to set down his methods and tells of the results that he has obtained. In general he is frank and states that few patients can be cured by individual effort, since it requires the teamwork of a specialized hospital in which physicians, nurses, orderlies and occupational therapists work together to improve the patient's condition.

The last point is worth reiteration, although it has been widely recognized since World War I. One of the plans of the late Harvey Cushing was to develop an institution along these lines, but the plan was thwarted by the difficulty in having patients centralized in such a large country as the United States. It is hoped, however, that such a plan may come into effect after the present crisis, since, thanks to increased facilities for the transportation of patients, the country is no longer so large as it was in 1920. Patients are now easily moved by aeroplane, and one can visualize a great hospital in such a central place as Chicago, with patients coming from all parts of the country.

Occupational Tumors and Allied Diseases. By W. C. Hueper, M.D. 4°, cloth, 896 pp. Springfield, Illinois: Charles C Thomas, 1942. $8.00.

This monograph provides an extensive and well-organized source of information concerning the various aspects of neoplastic lesions and allied diseases of probable occupational origin. After a discussion of the history, concepts and significance of these particular tumors the material is arranged by sections, corresponding to the systems of the body that are involved. Stress is laid on lesions of the skin, respiratory, alimentary and urinary systems, blood-forming organs and mesenchymal tissues. There is detailed information concerning the nature and source of the exciting and accessory etiologic agents. The histologic features, symptoms, diagnosis and treatment of the tumors in question are discussed comprehensively. The book closes with chapters on the relation of occupational neoplasms to the theories of carcinogenesis and on the medicolegal and public-health aspects of the problem. There is an extensive bibliography; the total number of references is well over 3500, and it is obvious that little of importance has been omitted. This in itself greatly enhances the value of the book.

Throughout, the author attempts to sift the available data and theoretical concepts of these tumors and to analyze and integrate the material to provide a coherent picture of each specific lesion. Aside from a few contradictions, it may be said that he has admirably succeeded in a most difficult task.

Frequently, the sentences are excessively long and complicated, which distracts one from the picture the author wishes to create. Furthermore, a summary of the pertinent material at the end of each chapter would be extremely helpful. The subject index, although adequate, would greatly improve the value of the book if it were more complete.

The incidence of occupational tumors has increased considerably as a result of the rapid development of industry in the last few decades. Consequently, a knowledge of these diseases is of extreme importance, and hence this monograph fulfills a definite need. Because of its wide scope, it can be recommended for all physicians and others who have to deal with industrial disease. The author and the publisher are to be congratulated on their painstaking work in the preparation of this volume.

Roentgen Treatment of Diseases of the Nervous System. By Cornelius G. Dyke, M.D., and Leo M. Davidoff, M.D. 8°, cloth, 198 pp., with 12 engravings, 7 charts and 16 graphs. Philadelphia: Lea and Febiger, 1942. $3.25.

This is an important book on a subject little understood. Only in the last decade or two have there been a sufficient number of cases of diseases of the nervous system under observation in one clinic, treated by adequate doses of roentgen rays and followed for a number of years for an evaluation of this type of therapy to be made. The senior author, Dr. Dyke, is radiologist to one of the largest neurological centers in this country, and the junior author, Dr. Davidoff, has long been recognized as an outstanding neurosurgeon, trained in the clinic of the late Harvey Cushing.

Over half the book deals with brain tumors. Each type of tumor is considered separately. The data on a number of treated cases are followed by one or two selected case histories and a general discussion of the effects of roentgen rays on the type of tumor under consideration. Each section is accompanied by graphs illustrating the amount of treatment, the time when it was given and the reaction of the patient. The amounts are given in totals, not in individual doses. Thus, by knowing the type of tumor, rapid information can be found in this book in regard to the use of roentgen rays as a form of treatment.

Another section of the volume deals with the treatment of spinal-cord tumors, infectious and inflammatory diseases, and miscellaneous conditions. A preliminary section of the book gives the technic of roentgen-ray treatment as developed in various centers in this country.

The book is thus a complete, up-to-date treatise on the subject, with a good working bibliography and an excellent index. To all neurosurgeons, neurologists and radiologists, this book is highly recommended.

(Notices on page viii)

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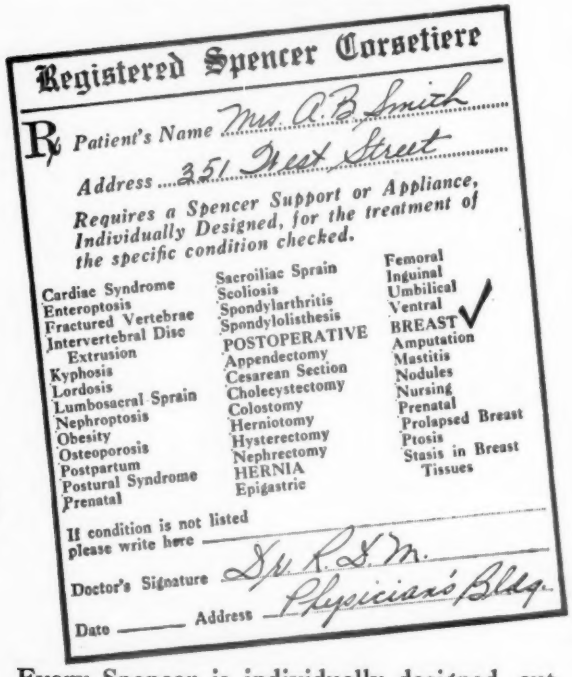

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NOTICES

ANNOUNCEMENT

Dr. Jacob F. Deich announces the removal of his office from 485 Commonwealth Avenue to 475 Commonwealth Avenue, Boston.

SOCIETY MEETINGS AND CONFERENCES

Calendar of Boston District for the Week Beginning Thursday, June 10

Thursday, June 10
•10:00–11:30 a.m. Medical staff rounds. Peter Bent Brigham Hospital.

Tuesday, June 15
2:00–4:00 p.m. Myasthenia gravis clinic. Out Patient Department, Massachusetts General Hospital.

Wednesday, June 16
•12:00 m. Clinicopathological conference. Children's Hospital.

•Open to the medical profession.

District Societies

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July 28.

BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

Laugh at the Lawyer Who Cross-Examines You! By Charles L. Cusumano, LL.B., of the New York Bar. 8°, cloth, 375 pp. New York City: Old Faithful Publishing Company, 1943. $3.00.

A practical manual written for those who must appear in court as witnesses. There is a chapter on the expert witness in which a subdivision is devoted to the physician. The book is based on experience, not theory, and contains much information and many suggestions of sound value.

The Principles and Practice of Obstetrics. By Joseph B. DeLee, M.D., consultant in obstetrics, Chicago Lying-in Hospital and Dispensary and consultant in obstetrics, Chicago Maternity Center; and J. P. Greenhill, M.D., attending obstetrician and gynecologist, Michael Reese Hospital, obstetrician and gynecologist, Associate Staff, Chicago Lying-in Hospital, attending gynecologist, Cook County Hospital, and professor of gynecology, Cook County Graduate School of Medicine. Eighth edition. 4°, cloth, 1101 pp., with 1074 illustrations. Philadelphia and London: W. B. Saunders Company. 1943. $10.00.

This eighth edition of an authoritative textbook, first published in 1913, has been thoroughly revised by Dr. Greenhill and entirely reset by the publisher. Two years before Dr. DeLee died, he asked Dr. Greenhill to prepare the eighth edition of his book, and nearly all the additions, deletions and corrections received Dr. DeLee's approval.

Among the major changes is a rearrangement of the material in the first third of the book. This was done to

(Books Received continued on page xiii)

avoid the slight confusion in the sequence of chapters in the previous editions. Another important change is the substitution of the English terms for the Latin ones in the designation of presentation and position. New chapters or sections have been added dealing with obstetric and gynecologic endocrinology, the use of vitamin K in obstetrics, erythroblastosis foetalis, vitamins and minerals, roentgenography in obstetrics, the sulfonamide drugs in obstetrics, and the Waters extraperitoneal cesarean section.

Several chapters and sections have been completely rewritten, notably those on the toxemias of pregnancy, in which is given the new classification proposed by the American Committee on Maternal Health; contracted pelves, from which the old classifications have been omitted and the new ones of Caldwell, Moloy, and d'Esopo and Thoms included; puerperal infection, in which the sulfonamides are discussed; pyelitis, including the use of the sulfonamides; the acute infections; analgesia and anesthesia; the use of pituitary extract and ergot; and the indications for and contraindications to cesarean section. Many of the old illustrations have been omitted, and a large number of new ones added.

The Sight Saver. By C. J. Gerling. 8°, cloth, 202 pp. New York: Harvest House, 1943. $2.00.

A popular manual on the hygiene of the eyes in which the various subjects are arranged alphabetically. This work attempts to combat the quackery and fraud existing today, and it covers sight conservation from every angle without encroaching on the family physician or eye specialist.

Diseases of the Skin. By Oliver S. Ormsby, M.D., Rush Professor of Dermatology, University of Illinois, and attending dermatologist to the Presbyterian Hospital of Chicago; and Hamilton Montgomery, M.D., associate professor of dermatology and syphilology, University of Minnesota (Mayo Foundation), and associate in the Section on Dermatology and Syphilology, Mayo Clinic. Sixth edition. 4°, cloth, 1360 pp., with 654 figures containing 723 illustrations and 6 colored plates. Philadelphia: Lea and Febiger, 1943. $14.00.

This ninth edition of a standard textbook on dermatology has been thoroughly revised in the light of recent knowledge. The book has been kept to a reasonable size by eliminating much material rendered obsolete by recent investigation. A large number of diseases have been regrouped, two new classes and twenty-two diseases not previously described in this text have been added. Many chapters have been rewritten.

Clinical Diagnosis by Laboratory Methods. A working manual of clinical pathology. By James C. Todd, M.D.; and Arthur H. Sanford, M.D., professor of clinical pathology, University of Minnesota (Mayo Foundation), and head of Division on Clinical Laboratories, Mayo Clinic. Tenth edition. 8°, cloth, 911 pp., with 380 illustrations. Philadelphia and London: W. B. Saunders Company, 1943. $6.00.

First published in 1908, this book on clinical pathology has attained a high position in its particular field. Much new material and a number of new illustrations have been added, and there is a new arrangement of the rickettsial diseases. There is a discussion of the significance of porphyrins in the urine and of methods for determining the quantity of sulfonamides and sulfones in the blood and for the identification of sulfonamide crystals in the urine. The significance of various inclusion bodies is considered, as well as hemoconcentration. Diseases due to fungi are mentioned, and Brewer's new methods for growing anaerobic organisms are described. A number of new methods have been added to the chapter on clinical chemistry. The Mazzini serum test and the Quick prothrombin test have been included. There are seventy-two new illustrations and four plates.

The Medical Clinics of North America. Symposium on Nutrition (March, 1943). Vol. 27, No. 2. 8°, cloth, 327 pp. Philadelphia and London: W. B. Saunders Company, 1943. $3.00.

A Surgeon's Fight to Rebuild Men: An autobiography. By Fred H. Albee, M.D. With a foreword by Lowell Thomas. 8°, cloth, 349 pp., with 10 illustrations and a frontispiece. New York City: E. P. Dutton and Company, Incorporated, 1943. $3.50.

This is an autobiography of a prominent American orthopedic surgeon.

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